

The Reliability of Ponderal Index in Predicting Short-Term Complications of Small for Gestational Age Term Infants.

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Research Article

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Abstract

The birth weight (BW) for gestational age (GA) ensure a fair assessment of the nutritional status of small for gestational (SGA) infants. Ponderal index (PI) is used to identify wasting. This study aims to evaluate the association between PI values and short-term complications of term SGA infants and evaluate the reliability of PI. A total of 489 term SGA infants were included in this retrospective study. According to the PI values, the neonates were divided into three groups. Group 1 consisted of infants with low PI (PI < 10th percentile) (n=45), group 2 consisted of infants with appropriate PI (PI 10th-90th percentile) (n=405) and the ones with high PI (PI > 90th percentile) (n=39) constituted group 3. Demographic and clinical data of the mothers and neonates including clinical and laboratory assessments were collected and compared statistically. No difference was observed between the groups other than the incidence of hypoglycemia, jaundice requiring treatment and hospitalization rate, which were all significantly higher in low PI group than the group 2 and 3 (p=0.01, p=0.006 and p=0.04, respectively). None of the babies had severe morbidity or died.

Conclusion: Although short-term complications were higher in term SGA infants with low PI, all term SGA infants should be defined as high-risk neonates and deserve special neonatal care and surveillance to prevent short-term complications.

What Is Known

- Ponderal index (PI) is an indicator to assess the growth pattern of SGA infants to determine the degree of fetal malnutrition.
- Ponderal index allows the differentiation between symmetric and asymmetric growth restriction.

What is New

- We showed that term SGA infants with low PI had higher risk of hypoglycemia, jaundice requiring treatment and hospitalization rate than SGA infants with appropriate or high PI.
- Ponderal index calculation can be a simple and beneficial tool to predict SGA infants who need to be observed closely

Introduction

Newborn weight and length values at birth reflect the quality and quantity of growth of the fetus in utero [1]. Fetal growth restriction (FGR) described as “all conditions leading to a marked reduction in size during intrauterine life” is linked to reduced birth weight (BW) [2]. The term of small for gestational age (SGA) is used to describe infants with a BW below the 10th percentile for that gestational age (GA) [3]. The estimated rate of SGA is approximately 10% of term infants in developed countries and 20% of term infants in developing countries [4]. Although FGR and SGA are mostly used as synonyms, they refer to different concepts. FGR is characterized with the lower fetal growth pattern than the expected growth

potential of an infant as a consequence of a perinatal insult. However, at birth these infants may have an appropriate BW as per GA. Thus, FGR infants are the ones with clinical evidence of malnutrition [5]. Hence, low birth weight itself does not include information about the neonate's body proportionality and it is not an enough parameter to define growth restriction. During pregnancy, depending on the time of the insult, growth-restricted infant may have symmetric or asymmetric growth restriction. If both the weight and length of the neonate are affected, it is defined as 'proportionately' or 'symmetrically' growth-restricted neonate. Proportionately growth restriction results mostly from genetic, infectious or teratogenic insult early in utero. On the other hand, the infants having low BW with normal birth length (BL) are defined as 'disproportionately' or 'asymmetrically' growth-restricted neonate which occurs in the later period of pregnancy as the result of hypoxemia and malnutrition due to placental insufficiency [6, 7]. It should be kept in mind that, a neonate with a BW less than 10th percentile may be an SGA infant but may not have FGR, on the other hand, a neonate with a BW greater than 10th percentile may have FGR [8]. However, both of these sets of neonates are reported to have higher morbidity and mortality rates than that of normal BW infants. Moreover, during childhood they may have greater risk for metabolic syndromes, neurologic and developmental delays [9].

Ponderal index (PI) is an indicator to assess the growth pattern of SGA infants to determine the degree of fetal malnutrition. It allows the differentiation between symmetric and asymmetric growth restriction. In addition, it evaluates the severity of asymmetry in growth restricted infants. It is determined by the ratio of BW to BL [6, 10]. According to the curves used, neonates below either the 3rd or 10th percentile for GA considered as fetal malnutrition or severe fetal wasting. Infants with asymmetrical SGA have a lower PI which is associated with higher rates of morbidities such as hypoglycemia, polycythemia, early hyperbilirubinemia, hypothermia, perinatal resuscitation, perinatal asphyxia, fetal distress or long hospital stay in the neonatal period [11, 12].

The aim of this retrospective study was to determine the association between PI values and short-term complications of SGA term infants and evaluate whether low PI is associated with higher morbidity.

Material And Methods

This is a retrospective study of singleton live births from January 2007 through May 2017, using the medical records of pediatrics department of the hospital. These records contain information on maternal and neonatal demographics. The present study was executed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the university hospital.

Medical records of all newborns born in that period (n=11,938) were reviewed. Babies born to mothers who had pathologies affecting the intrauterine growth of the fetus such as infants of diabetic mother and infants born to preeclamptic mother were not included. The neonates having the clinical evidence of chromosomal abnormality, gross congenital abnormalities or lethal malformations, stillbirths, multiple births and those with uncertain GA were excluded.

In all cases, the calculation of GA was based on the date of the last menstrual period of the mother and ultrasound performed in the first trimester of pregnancy. BW, BL and head circumference (HC) were determined on arrival in the nursery and performed by the neonatal nurses. BW was measured by using an electronic scale (Seca 354) calibrated to 10 g. To determine the BL, the result of the measurement of crown-heel length performed by a portable infantometer (Seca) with a range 1 to 75 cm, calibrated to 1 mm was used. HC was measured with a tape encircling the head in the frontal area above the glabella and most prominent portion of the occiput posteriorly. Term infants (37-42 weeks) whose BW were below 10th percentile according to the growth curves for Turkish population were considered as SGA infants and included in the study [13]. Of the 495 neonates, 6 of them were excluded due to congenital heart anomaly (n=4), diaphragmatic hernia (n=1) and omphalocele (n=1). Finally, a total of 489 SGA infants were included in the study.

PI was calculated by the following formula:

$$PI = \frac{\text{birthweight in grams} \times 100}{\text{length}^3 \text{ in centimeters}}$$

PI of SGA infants were plotted on the percentile curves of Miller and Hassanein [14]. According to the PI values, the neonates were classified as low PI (PI < 10th percentile), appropriate PI (PI 10th-90th percentile) and high PI (PI > 90th percentile) and defined as group 1, group 2 and group 3, respectively.

Other data collected included information regarding gender, mode of delivery, the need of perinatal resuscitation, 5th minute APGAR score, body temperature (°C) on admission, jaundice requiring treatment, respiratory distress, hospitalization and rehospitalization rates, hospitalization duration, degree of weight loss (%), the need of noninvasive ventilation, the lowest blood glucose level, complete blood count, and thyroid function tests. Hypothermia was defined as axillary body temperature below 36 °C [15]; hypoglycemia as a blood glucose concentration below 45 mg/dL [16]; polycythemia as a venous hemoglobin level exceeding 22 g/dL [17]; neutropenia as the absolute neutrophil count less than 1000 cells/mm³ [18]; thrombocytopenia as platelet count less than 150,000/mm³ [19].

We used the SPSS software for Windows, version 20.0 (SPSS Inc., Chicago, IL, USA) for statistical analyses. The variables were investigated using visual (histograms, probability plots) and analytical methods (Shapiro-Wilk test) to determine if they are normally distributed. Descriptive analyses were presented using means±SD for normally distributed variables, as medians (range, 25–75 p) for the nonparametric variables and as percentages for categorical variables. Normally distributed variables were compared by One-way Anova, nonparametric variables by Friedman test, and categorical variables by chi-square test. Spearman's correlation analysis was performed to detect any correlation between the GA and PI of the infants. P < 0.05 was considered to indicate a significant difference.

Results

Of the 11,938 neonates, there were 555 (4.6%) SGA infants, 495 of them were term babies. After excluding 6 infants due to congenital anomalies, group 1 consisted of 45 neonates (9.2%) whose PI was below 10th percentile whereas, 405 neonates (82.8%) with a PI between 10th and 90th percentile and 39 neonates (8%) with PI above 90th percentile constituted group 2 and 3, respectively. The demographic characteristics of group 1, group 2 and group 3 SGA infants are shown in Table 1. Incidence of hypoglycemia, jaundice requiring treatment and hospitalization rate were significantly higher in infants with low PI (group 1) ($p = 0.01$, $p = 0.006$ and $p = 0.04$, respectively). Adverse outcomes and morbidity pattern of the study groups are demonstrated in Table 2. There was a significant inverse correlation between the blood glucose and bilirubin levels of the babies ($r = -0.28$, $p < 0.001$). That is, as blood glucose levels of the babies increased, bilirubin levels decreased. Complete blood count was obtained only from 61 infants (Table 3). Thrombocytopenia was observed in 45.5% of infants in group 1 and 22.2% and 20% of the infants in group 2 and 3, hence the difference was not statistically significant. Only five infants in group 2 had polycythemia. Five infants had a body temperature below 36°C who were also in group 2. However, both morbidities which were only observed in group 2 had no statistical significance.

Table 1
Baseline characteristic of the study groups

| Parameters | Group 1 (PI < 10 P) (n = 45) | Group 2 (PI 10–90 P) (n = 405) | Group 3 PI > 90 P (n = 39) | p value |
|-----------------------------------------------------|------------------------------------|--------------------------------------|----------------------------------|---------|
| Gestational weeks, mean \pm SD | 38.7 \pm 1.1 | 38.9 \pm 1.13 | 38.6 \pm 1 | 0.06 |
| Weight (g), mean \pm SD | 2410 \pm 338 | 2630 \pm 218 | 2635 \pm 153 | < 0.001 |
| Length (cm), mean \pm SD | 47.9 \pm 2.5 | 46.9 \pm 1.5 | 44.6 \pm 1.2 | < 0.001 |
| Head circumference (cm), mean \pm SD | 32.8 \pm 1.6 | 33.3 \pm 1.1 | 33.1 \pm 1 | 0.02 |
| Ponderal index, mean \pm SD | 2.2 \pm 0.1 | 2.5 \pm 0.14 | 2.96 \pm 0.17 | < 0.001 |
| Male gender, n (%) | 15 (33.3) | 142 (35.1) | 10 (25.6) | 0.5 |
| C-section, n (%) | 32 (71.1) | 288 (71.1) | 27 (69.2) | 0.97 |
| Perinatal resuscitation in the delivery room, n (%) | 1 (2.2) | 11 (2.7) | 2 (5.1) | 0.7 |
| 5th minute APGAR score, median (25–75 p) | 10 (10–10) | 10 (10–10) | 10 (10–10) | 0.2 |

Table 2
Adverse outcomes and morbidity pattern of the study groups

| Parameters | Group 1 (PI < 10 P) (n = 45) | Group 2 (PI 10–90 P) (n = 405) | Group 3 (PI > 90 P) (n = 39) | p value |
|-----------------------------------------------------|------------------------------------|--------------------------------------|------------------------------------|---------|
| Jaundice needed to be treated, n (%) | 8 (17.8) | 24 (5.9) | 1 (2.6) | 0.006 |
| Respiratory distress, n (%) | 3 (6.7) | 14 (3.5) | 1 (2.6) | 0.5 |
| Hospitalization, n (%) | 7 (15.6) | 24 (5.9) | 2 (5.1) | 0.04 |
| Rehospitalization, n (%) | 5 (11.1) | 41 (10.1) | 7 (17.9) | 0.3 |
| Perinatal resuscitation in the delivery room, n (%) | 1 (2.2) | 11 (2.7) | 2 (5.1) | 0.7 |
| Percentage of weight loss (%) | 7.1 ± 2.6 | 6.8 ± 2.2 | 6.9 ± 2.7 | 0.6 |
| Noninvasive ventilation, n (%) | 2 (4.4) | 6 (1.5) | 0 | 0.2 |
| Hypoglycemia, n (%) | 18 (45) | 90 (24.2) | 7 (18.9) | 0.01 |
| TSH level (mIU/L), median (25–75 p) | 7.2 (5.3–15.2) | 6.6 (3.6–10.6) | 7.6 (3.8–10.6) | 0.3 |

Table 3
The results of the laboratory findings of the term SGA infants in all groups

| Parameters | Group 1 (n = 11) | Group 2 (n = 45) | Group 3 (n = 5) | p value |
|--------------------------------------------------------|---------------------------|----------------------------|----------------------------|---------|
| Hemoglobin (g/dL) | 17.8 ± 2.1 | 17.9 ± 2.8 | 15.1 ± 2.2 | 0.09 |
| Leucocytes (/mm ³), median (25–75 p) | 15.360 7620 – 17.760 | 13.600 11.490-20.965 | 11.470 8780 – 29.910 | 0.8 |
| Neutrophil count (/mm ³), median (25–75 p) | 6385 3163-13.729 | 8500 5704-13.665 | 5510 4655-12.575 | 0.6 |
| Platelet count (/mm ³), median (25–75 p) | 167.000 96.000-288.000 | 242.000 172.500–283.000 | 216.000 151.500-239.500 | 0.38 |
| Thrombocytopenia, n (%) | 5 (45.5) | 10 (22.2) | 1 (20) | 0.28 |

None of the babies had severe morbidity or died. Nine infants (1.84%) had meconium-stained amniotic fluid, but only one was hospitalized due to meconium aspiration and another one due to perinatal

asphyxia both of whom had PI of 10th -90th percentile.

There was no correlation between the GA and PI values ($r = 0.018$, $p = 0.69$).

Discussion

Suboptimal fetal growth resulting in an SGA infant or FGR is an important issue which is linked to increased morbidity and mortality rates, decreased lifespan as well as increased cost of care. Approximately five decades ago, it was reported that SGA infants born at term gestation had 6-fold increased risk for neonatal mortality and 3-fold increased risk for neonatal morbidities compared with the term appropriate for gestational age (AGA) infants [20]. Previous studies have shown that asymmetric SGA infants (infants with $PI < 10$ th percentile) have higher neonatal morbidity than symmetric SGA infants (infants with $PI > 10$ th percentile) in terms of acute neonatal consequences including metabolic and hematological disturbances plus disrupted thermoregulation [1, 4]. In this study, we showed that term SGA infants with low PI had higher risk of hypoglycemia, jaundice requiring treatment and hospitalization rate than SGA infants with appropriate or high PI. None of the infants died or had a life threatening complication due to growth restriction.

SGA infants face with many different medical problems after birth. The infants who are severely affected, deprived of oxygen and nutrients, may have difficult cardiopulmonary transition and develop perinatal asphyxia, meconium aspiration or persistent pulmonary hypertension. Due to respiratory distress, gastrointestinal problems, metabolic and hematologic disturbances, the hospitalization rates are higher in SGA infants than AGA infants [1, 12, 21]. Among our subjects, only one developed perinatal asphyxia but none developed persistent pulmonary hypertension. Although nine infants had meconium-stained amniotic fluid, only one of them with an appropriate PI developed meconium aspiration syndrome. However, in our study, hospitalization rates of SGA infants with low PI (15.6%) were higher than the infants with appropriate and high PI (5.9 and 5.1%, respectively) ($p = 0.04$).

Hypothermia is another common complication that can be observed in these infants due to inadequate measures of temperature control. Relatively large body surface area, low body and subcutaneous tissue fat, impaired thermoregulation and catecholamine consumption plus simultaneous occurrence of hypoglycemia and hypoxia are the main causes of hypothermia [12, 21, 22]. In this study hypothermia was only observed in five infants, all of whom had appropriate PI (group 2) which was not statistically significant.

In the first days of life, as a consequence of delay in postnatal metabolic adaptation, hypoglycemia becomes a major concern for SGA infants. It can be observed due to low glycogen stores, decreased gluconeogenesis, increased sensitivity to insulin, low fat and decreased ability to oxidize free fatty acids and triglycerides. In addition, perinatal asphyxia, polycythemia and hypothermia can exacerbate hypoglycemia [12, 21, 23]. The results of many reports recommend screening of SGA infants in the first 24 hours of life. There is no single set blood glucose concentration below which hypoglycemia is linked to neurologic deficit. According to AAP, the target plasma glucose concentration should be 45 mg/dL or

higher for all infants [16]. Doctor et al. [9] compared 372 SGA infants with the same number of AGA infants and demonstrated that SGA infants had significantly higher rates of hypoglycemia (5%) than AGA infants (1%). Deorari et al. [24] noticed that, of the 144 SGA infants, 24 (17%) of them developed hypoglycemia. Moreover, the ones whose BW was < 3th percentile (n = 12) had higher risk (25.5%) than the ones whose BW was between 3th -10th percentile. Nili et al. [11] conducted a study with 361 term SGA infants and reported that hypoglycemia was higher in the term SGA infants with low PI group than the infants with appropriate and high PI which was statistically significant. In the present study, the incidence of hypoglycemia was the highest in infants with low PI; 45% of these infants had hypoglycemia in this group and hypoglycemia was the lowest in infants with PI over 90th percentile (18.9%), which was statistically significant (p = 0.01). This result is rational; hence PI of babies increase as the BW increases, thus providing more glycogen stores to the babies.

Jaundice (indirect hyperbilirubinemia) is known to be associated with growth restriction in term infants which may be due to decrease in liver size and immaturity of liver function [25, 26]. In this study, we demonstrated that the rate of jaundice requiring phototherapy was 17.8% in low PI SGA infants which was higher than the other two groups (5.9 and 2.6% in infants with appropriate and high PI, respectively) and was statistically significant (p = 0.006).

We only included term babies in our study and therefore found no correlation between the GA and PI, though PI values increase as GA of the infants increase, they remain constant after the 37th week of gestation [14].

The present study has some limitations. First, the measurements were performed by several newborn nurses and the study is retrospective which may explain the discrepancy among the groups. Secondly, maternal socio-cultural and socio-economic levels were higher that may not reflect normal population. In addition, the data on maternal characteristics and the records of maternal weight gain during pregnancy were not available which would determine an association between poor maternal weight gain and low PI.

In conclusion, in the present study we demonstrated that SGA infants with PI levels less than 10th percentile have higher short-term complications including hypoglycemia, jaundice requiring treatment and hospitalization rate than other SGA infants. However, independent of PI, all SGA infants should be considered as a high-risk neonate and should be monitored closely for early identification of any short-term complication during the neonatal period. In this study, there is no data about the long-term outcomes of these infants. It is also recommended to follow-up all SGA infants including low PI infants in terms of neurologic, cognitive and metabolic outcomes in the long term and evaluate these babies according to their long term outcomes also.

Abbreviations

AGA Appropriate for gestational age

BL Birth length

BW Birth weight

FGR Fetal growth restriction

GA Gestational age

HC Head circumference

PI Ponderal index

SGA Small for gestational age

Declarations

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Conflicts of interest/Competing interests The authors have no conflicts of interest to declare that are relevant to the content of this article.

Availability of data and material Not applicable

Code availability Not applicable

Authors' contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Secil Ercin, Yesim Coskun and Tugba Gürsoy. The first draft of the manuscript was written by Secil Ercin and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval Ethical approval was waived by the local Ethics Committee Koç University School Of Medicine in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Consent to participate Written informed consent was obtained from the parents.

Consent for publication Patients signed informed consent regarding publishing their data and photographs.

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