Characteristics of the SGA children in the placenta biobank at Örebro University Hospital

Version 2

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Abstract

Introduction: Being born SGA is defined as being born at or below –2 SD and it is associated with mortality and morbidity during the perinatal period and during later life. Several factors has an impact on risk of a being born SGA such as maternal and fetal factors as well as exposure to toxins and endocrine factors.

Aim: We wanted to describe the characteristics of SGA children regarding several different risk factors and also compare the SGA children to AGA children.

Material and Method: Clinical data was collected from 6,801 subjects during the years 2007-2012 were 293 subjects was born SGA and 6,508 was born AGA. Information concerning the mother’s health and the child’s characteristics was extracted from medical records.

Results: The SGA children was more often born males (p = < 0.001), born twins (p = < 0.001), born through a complicated vaginal or through caesarean section (p = < 0.001), born at a lower gestational age (p = < 0.001) and had a lower Apgar score at one, five and ten minutes (p = < 0.001) than AGA children. Their mothers had a higher prevalence of smoking at registration at maternal health care (p = < 0.001) as well as during gestational week 30-32 (p = .040) and a higher frequency of lower gestational weight gain (p = < 0.001). No difference between the SGA children and AGA children was seen according to the mother’s pre-pregnancy BMI (p = .070) or their age at delivery (p = .469).

Conclusion: Significant differences among several factors was found when comparing SGA children to AGA children such as gestational weight gain, gestational age, Apgar score, twin birth and smoking during pregnancy, concordant to earlier studies. Furthermore, male gender was a risk factor for being born SGA which has not previously been recorded. Further research on whether gender is a risk factor among other populations is suggested.
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**Introduction**

Individuals born small for gestational age (SGA) are at higher risk of mortality and morbidity during perinatal life as well as during later life [1]. Consequences of being born SGA includes short stature, metabolic alterations and health problems, such as the metabolic syndrome, glucose intolerance, stroke, airway disease, disorders of onset of puberty, liver cirrhosis, and renal disease [2-9].

A study investigating mortality and morbidity in relation to birth weight found that babies born at full term but at or below the 3th percentile had a 10 times higher risk of neonatal death compared to their normal weight peers as a result of higher risk of sepsis and seizures during neonatal period. Also, the Apgar score was significantly lower in children with low birth weight, especially children born below the 3th percentile [10]. Apgar score is a tool introduced during the 1950’s that since then has been used to assess the newborn child’s health state and to predict neonatal outcome [11]. This method, as Brian W. casey et al claims ”continues to be relevant to the prediction of neonatal outcome after almost half a century” [12].

In later life, a comparison between average for gestational age (AGA) and SGA children showed that SGA children at age nine years had significantly lower insulin sensitivity [3]. The metabolic syndrome is much more prevalent in children born SGA than in children born AGA (2.3 % vs. 0.3%). This increase is above all due to a higher insulin resistance in children born SGA [13]. Also later in life, at age 22 years and 30 years, individuals born SGA exhibit both higher insulin resistance and a higher prevalence of the metabolic syndrome compared to those born AGA [4].

SGA is defined as having a birth weight or birth length that is two standard deviations (SD) or more below the expected weight or length for the child’s gestational age in relation to a reference population [1]. Minus 2 SD is the most used cut off level with the following motivation: ”-2 sd is likely to capture the majority of infants with impaired fetal growth” [1]. However, SGA is sometimes defined as having a birth weight or birth length below the 3rd, 5th, or 10th percentile for gestational age [1]. Defining SGA by the 10th percentile would include infants that are healthy but small and is therefore not sensitive enough for identification of fetuses with restricted intrauterine growth [14].
SGA is classified into three separate groups depending on which body dimension that is reduced:
1. SGA with birth weight < -2 SD
2. SGA with birth length < -2 SD
3. SGA with both birth length and weight < -2 SD [15,16]

Neonates that are SGA of any type and also have small head circumferences should be particularly recognized because they have an increased risk of developing a cognitive impairment, especially if they lack sufficient catch-up growth [2].

However, the definition is not straightforward and the cut off level used differs in different studies. The SGA definition requires three parts:
1. A precise gestational age which should be based on an ultrasound dating rather than menstrual dating since this is not as accurate and often results in an incorrect flattening of the growth pattern and leads to false post-term deliveries [17,18].
2. Accurate measurements at birth of weight, length, and head circumference.
3. A well-studied cut off level that is compared to an appropriate reference population [2].

Furthermore, the definition does not take into account different background factors that may influence intrauterine growth. These factors include maternal size, ethnicity, and parity. When included, a more correct diagnosis of intrauterine growth restriction (IUGR) can be done [2]. Therefore, a new definition of the concept of SGA birth has been proposed: "For epidemiological analysis as well as for prospective assessment of fetal growth, individual adjustments of weight limits reduce false-positive results and help to identify those babies who are pathologically small. This should lead to improved screening and further investigation (especially by Doppler analysis) of those babies who are at risk." [17]. There are several factors that should be taken into consideration when judging whether a newborn infant as pathologically small or not, such as "maternal height, weight in early pregnancy, parity and ethnic group, as well as the sex of the baby. Paternal height also plays a role, but this is relatively minor." [17].

A study was performed in 1992 in Gothenburg where 3,650 pupils in the final grade were examined regarding their birth weight and birth length with the aim of finding children born SGA and clarifying the risk of being short later in life due to SGA birth. One hundred and ninety-eight children (5.5%) were found to have been born SGA by any of the three definitions above [5].
Another study performed by Mary L. Hediger et al [19] including 4,431 study subjects showed that 8.6% of the children was born SGA. The 10th percentile was used as the cut off level in this study.

Most children born SGA (> 80%) do not stay below the cut off level of < - 2 SD in length, but experience a catch-up growth and achieve a normal final height above - 2 SD. The catch-up growth is most often an early postnatal process that takes place during the first six months of life and is completed when the child turns two years of age [1,5]. However, the process can be prolonged to approximately four years of age when the child is both preterm and SGA [15]. Children born SGA reach final heights that are approximately - 1 SD compared to the normal population [2]. However, 10-15% of the children born SGA do not undergo a period of catch-up growth and therefore stay below - 2 SD during adulthood. Children born with length < - 2 SD have a higher risk of an insufficient catch-up process resulting in a lower final height than children born with weight < - 2 SD [15].

IUGR can easily be confused with SGA. These concepts are closely related but not the same. IUGR is a condition that prevents the fetus to reach its growth potential and it has a specific pathological cause. On the other hand, SGA is a statistical measurement of dimensions at birth compared to a predetermined cut off level in a reference material, which is specific to geographic location and ethnicity. A SGA baby is not always IUGR and a baby that has IUGR is not always born SGA [1,15]. A newborn that is constitutionally, but not pathologically, SGA does not have increased risks of morbidity and mortality compared to AGA newborn infants. It is infants born after IUGR that exhibit the increased risk of health problems described above both during the perinatal period and during adulthood. Therefore, it is important to identify children born after IUGR [14,20]. However, this may be difficult to achieve and it is easier to identify children born SGA.

**Etiology to SGA birth**

**Maternal nutrition and gestational weight gain**
Several factors have an impact on growth of the fetus. Low intake of nutrients and energy, and consequently low weight gain during pregnancy, has been shown to result in a child with normal birth length but modest birth weight [1]. The impact of maternal nutrition is probably less important in the western society than in poorer societies and may be hard to distinguish from other factors, such as social class [14]. Reasons for an inadequate gestational weight gain are e.g. age < 19 years, underweight during the pre-pregnancy period and ethnicity [21]. The recommendation for weight
gain during pregnancy differs depending on the maternal pre-pregnancy body mass index (BMI). The lower the BMI the larger the gestational weight gain should be [22].

**Fetal nutrition and placenta**
Normal growth of a fetus is dependent on a good nutritional environment. An intra-uterine environment that does not provide enough nutrients will alter both qualitative and quantitative growth of the fetus. A poor nutritional environment can be caused by an insufficient nutritional intake by the mother, maternal sickness or a dysfunctional placenta [14,18]. Multiple pregnancies have a five to ten-fold higher risk for IUGR compared with singleton pregnancies, 15-30% of twin pregnancies lead to IUGR [23,24]. Pregnancies with multiple fetuses generally generate children with lower birth weight [1].

**Exposure to toxins**
Smoking is a major factor that restricts the growth of the fetus. Research states that per cigarette smoked daily during the pregnancy, the birth weight is reduced by 13 grams [14]. Passive smoking has also been shown to expose the fetus to nicotine metabolites almost to the same extent as active maternal smoking [25]. A Japanese study showed that the risk of giving birth to a SGA child increased 2.8 times in mothers who smoked compared to mothers who did not smoke during the pregnancy [26].

**Endocrine factors**
Several endocrine factors are important for fetal growth. One of these factors is insulin-like growth factor (IGF II), which is an important regulator of fetoplacental growth [1,18,27,28]. Pro-IGF-II must undergo processing to generate the mature form of IGF-II. This process is catalysed by a proprotein convertas (PC4). Dysfunctional PC4 leads to low levels of mature IGF-II and restricted fetoplacental growth, which shows the important role for IGF-II in early fetal development [27]. Lower maternal levels of IGF-I and growth hormone (GH) during the third trimester have been found in pregnancies complicated with IUGR. However, the mechanism by which IGF-I and GH regulate fetal growth is unclear [1]. Mutations and alterations to the IGF-I-receptor have also been associated with SGA birth and it is believed that 2.5 % of all SGA children have alterations in the IGF-I-receptor [18,29]. Insulin and thyroxin are other endocrine factors that have an important role in fetal growth. For example, insulin levels in cord blood in children born SGA are lower than in children born AGA [28,30,31].
Aims
The aims of this study were to describe the characteristics of SGA children in a collection of placental biopsies at Örebro University Hospital, Örebro, Sweden, and to compare them with those of AGA children in the same collection. Furthermore, we aimed at investigating differences in the frequency of SGA birth in the sample collection.

Materials and methods
Study design
This study was a cross sectional epidemiological study.

Subjects and procedures
Placental biopsies, cord blood samples, and clinical data were collected from 11,651 subjects at Örebro University Hospital, Örebro, Sweden, during the period 2004-2012 with the aim to build a sample collection for studies on associations between inflammatory marker and fetal growth and preterm birth, the placenta study. The subjects were women who gave birth during the period at the Maternity ward, The Women’s Department, Örebro University Hospital, and who had been asked and approved in writing to participate in the study at the antenatal care units in Region Örebro County.

This study was based on the clinical data in that sample collection. These data include age and BMI of the mother, smoking during pregnancy, and birth z-scores of weight and length, Apgar score, gender, and gestational age of the child; delivery mode and whether the pregnancy was singleton or not. Information on use of tobacco was collected through the mother’s own statements made prospectively during routine antenatal care.

In 2008 an electronic medical record was introduced for each patient at the Women’s Department at Örebro University Hospital. In relation to that, the information collected for each subject in the placenta study was changed. This led to the existence of different background information for women giving birth during 2004-2007 and women giving birth 2008-2012. The background information for the period 2004-2007 needed completion. In this project, information for 395 of the 1,014 birth included in the placental study during year 2007 was completed thru retrieving the
medical records from the archive at The Women’s Department at Örebro University Hospital. The information was taken from the ordinary forms used during routine antenatal care and delivery in Sweden. The forms were included in the medical records. Factors completed was the mother’s weight at registration at maternal health and at the maternity ward, length at maternity ward, the child’s head circumference and length at birth, Apgar-score at five minutes, number of fetuses and smoking at registration at maternal health and at week 30-32 of pregnancy. The supplemented clinical data for 2007 was added to the existing data file, yielding a complete file with background data on 7,627 children born between 2007 and 2012. After screening for the definitions for SGA and AGA 6,801 cases was left meeting the criteria for the definition, as seen in Figure 1.

Children having a birth weight z-score < -2 were defined as being SGA in this study. Children having a birth weight z-score and a birth length z-score between -1.99 and 1.99 were defined as being born AGA in this study, Figure 1.

![Figure 1](image_url)

Figure 1. Flowchart of the selection of subjects in this study. Resulting in two groups, one fulfilling the definition for small for gestational age (SGA) and one fulfilling the definition for average for gestational age (AGA). N = Number.
The z-score for weight were calculated for all the years (2004-2012), but the z-scores for length were only calculated for the years 2008-2012 since data on birth length was missing for the years 2004-2007 when the z-score were calculated. The z-score were computed as shown in the paper of Aimond Nichlasson et al where birth weight and birth length are related to a reference population, gestational age and gender [32]. Therefore only weight z-score was included in the definition of SGA in this study.

Type of delivery was divided into four groups: uncomplicated, vaginal delivery; complicated, vaginal delivery; acute caesarean section, and planned caesarean section. Uncomplicated, vaginal delivery was defined as 1) Crown invitation, 2) No use of vacuum extraction, and 3) Vaginal delivery. A complicated vaginal delivery was defined as a vaginal delivery that did not meet the other two criteria required for an uncomplicated vaginal delivery.

Statistics
All analyses were performed using the software programme SPSS (Statistical Package for the Social Sciences), version 22. Tests for normality were made with a graphic analysis, comparing mean and median values and calculating the sum of subjects in each standard deviation since the study had a large number of subjects [33]. Because some of the data were normally distributed and some not, both parametrical T-Tests and non-parametric Mann-Whitney U test were executed. The results are presented as median (range) or mean (SD), where appropriate. For the non-numerical variables, the Chi-2 test was executed.

Ethics
The regional Ethical Board in Uppsala, Sweden, approved of the placenta study. That approval included the collection of background data and analyses done in this study. A certificate was written and approved by the head of The Women’s Department at Örebro University Hospital to meet the stringent directives for medical students of getting access to the medical records of patients.

Results
Of the eligible 7,627 children in the supplemented placenta sample collection, 293 fulfilled our criteria for being born SGA and 6,508 fulfilled our criteria for being born AGA, Figure 1.
Children in the sample collection born SGA according to the criteria used in this study had a lower gestational age (39.7 weeks vs. 40 weeks, \( p = < 0.001 \)), were more often boys (59.5% vs. 52%, \( p = < 0.001 \)), their mothers gained less weight during the pregnancy (SGA \( n = 188 \), AGA \( n = 4,613 \), 13 vs. 15, \( p = < 0.001 \)) and they were more often born as twins compared to singletons (8.9% vs. 1.8%, \( p = < 0.001 \)) than children born AGA.

There were significant differences in Apgar-scores at one, five and ten minutes between SGA and AGA children, Table 1.

**Table 1, Apgar-score at one, five and ten minutes for children born small for gestational age (SGA) and children born average for gestational age (AGA).** \( N = \) Number.

<table>
<thead>
<tr>
<th></th>
<th>Apgar-score 1 min</th>
<th>Apgar-score 5 min</th>
<th>Apgar-score 10 min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SGA ( N = 292 )</td>
<td>AGA ( N = 6503 )</td>
<td>SGA ( N = 293 )</td>
</tr>
<tr>
<td>Median</td>
<td>9</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Min</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Max</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>P-value</td>
<td>(&lt; 0.001)</td>
<td>(&lt; 0.001)</td>
<td>(&lt; 0.001)</td>
</tr>
</tbody>
</table>

The occurrence of smoking showed a significant difference between the SGA and AGA group, both at registration at maternal health care as well as during gestational week 30-32, see Table 2.

**Table 2, The percentage of smoking at registration at maternal health and at week 30-32 for mothers to children born small for gestational age (SGA) and children born average for gestational age (AGA).** \( N = \) Number.

<table>
<thead>
<tr>
<th>Smoking at registration at maternal health care</th>
<th>Smoking at gestational week 30-32</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA ( N = 284 )</td>
<td>SGA ( N = 246 )</td>
</tr>
<tr>
<td>AGA ( N = 6347 )</td>
<td>AGA ( N = 5953 )</td>
</tr>
<tr>
<td>No smoking</td>
<td>88,7%</td>
</tr>
<tr>
<td></td>
<td>93,7%</td>
</tr>
<tr>
<td>1-9 cigarettes per day</td>
<td>8,8%</td>
</tr>
<tr>
<td></td>
<td>4,8%</td>
</tr>
<tr>
<td>&gt; 10 cigarettes per day</td>
<td>2,5%</td>
</tr>
<tr>
<td></td>
<td>1,5%</td>
</tr>
<tr>
<td>P-value</td>
<td>(&lt; 0.001)</td>
</tr>
</tbody>
</table>
The SGA children were more often delivered through a complicated vaginal delivery or an acute caesarean section or a planned caesarean section than AGA children, Figure 2 ($p = < 0.001$).

![Figure 2. Percentage of each type of delivery mode for children born small for gestational age (SGA) and children born average for gestational age (AGA).](image)

Mothers to children born SGA did not differ significantly in age at delivery (29 years vs. 29.84 years, $p = 0.469$) or in pre-pregnancy BMI, (SGA $n = 278$, AGA $n = 6,139$, BMI 22.99 vs. BMI 23.59, $p = 0.070$) compared to mothers to children born AGA.

Table 3 shows the frequencies of SGA births and AGA births in the sample collection at Örebro University Hospital per year from the year 2004 to 2012. Definition used is only based on weight, AGA is defined as birth weight z-score between -1.99 and 1.99 and SGA is defined as birth weight z-score < 2.

Table 3, percentage of children born small for gestation (SGA) and children born average for gestational age (AGA) in the period 2004-2012. $N =$ Number.

<table>
<thead>
<tr>
<th>Year</th>
<th>SGA N (percentage)</th>
<th>AGA N (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>37 (3.8%)</td>
<td>929 (94.2%)</td>
</tr>
<tr>
<td>Year</td>
<td>SGA Children</td>
<td>Non-SGA Children</td>
</tr>
<tr>
<td>------</td>
<td>--------------</td>
<td>------------------</td>
</tr>
<tr>
<td>2005</td>
<td>47 (3.6%)</td>
<td>1242 (94.1%)</td>
</tr>
<tr>
<td>2006</td>
<td>38 (3.5%)</td>
<td>1033 (93.9%)</td>
</tr>
<tr>
<td>2007</td>
<td>44 (4.3%)</td>
<td>960 (94.7%)</td>
</tr>
<tr>
<td>2008</td>
<td>59 (4.2%)</td>
<td>1335 (94.3%)</td>
</tr>
<tr>
<td>2009</td>
<td>77 (4.0%)</td>
<td>1825 (94.5%)</td>
</tr>
<tr>
<td>2010</td>
<td>65 (3.5%)</td>
<td>1756 (94.4%)</td>
</tr>
<tr>
<td>2011</td>
<td>63 (3.7%)</td>
<td>1618 (94.6%)</td>
</tr>
<tr>
<td>2012</td>
<td>10 (3.4%)</td>
<td>294 (93.6%)</td>
</tr>
</tbody>
</table>

**Discussion**

This study’s aim was to describe what characterizes the SGA children in the placenta biobank at Örebro university hospital. Factors included were factors that usually are associated with the incidence of being born SGA or factors that are commonly associated with SGA children. Unfortunately we only had information on z-scores for weight, which made it impossible to compare the different type of SGA types; SGA for weight, SGA for length and SGA for both weight and length. This since SGA for length and SGA for weight and length need a z-score for length to be defined.

In the present study 3.8% of all subjects in the supplemented sample collection of children born 2004-2012 were SGA compared to 5.1% that K Albertsson-Wikland et al [5] and 8.6% that Mary L. Hediger et al [19] found in their studies. Reasons to these differences may be that in the present study the definition of SGA only including low weight excluding low length. Further research possibilities could be to investigate children born SGA for length and children born SGA for both length and weight as well, to more precisely survey the characteristics of the SGA children in the sample collection.

In accordance with previous findings we found increased smoking, insufficient gestational weight gain, lower Apgar score and a higher frequency of twin birth in children born SGA [1,18,22,24,26].

The recommended gestational weight gain differs depending on the mothers pre-pregnancy BMI. Grouping the mothers according to their BMI would probably have given more accurate results on the influence of gestational weight gain on SGA birth in each of these groups [22]. Hence, we can
only agree to previous studies that a non-sufficient gain of weight during pregnancy is a risk factor for giving birth to a SGA child.

Apgar score did differ amongst the SGA weight and AGA weight group concerning Apgar score at every occasion. This finding is consistent compared to the findings of Brian W. et al where lower birth weight was coupled to lower Apgar score at 5 minutes [10].

As expected, the occurrence of twins was more frequent among SGAW children than AGAW children, since twin pregnancy is associated with IUGR, which has associations with being born SGA [24].

Our results indicates that risk of giving birth to a SGA child is independent of when smoking is performed since the P-value for smoking during week 30 to 32 (P = 0,040) and the P value for smoking during beginning of pregnancy (p = < 0.001) is both significant. This is a risk factor that has a significant impact on the incidence of SGAW children and it is very much avoidable. A possible opportunity for further research could be to further investigate the amount of impact smoking has on the incidence of SGA children and how maternal health care deals with this issue. This factor had limitations in the material since in several cases information about tobacco use was missing. Although, significance was that great that even without these missing cases we can assume that smoking has a true impact on the outcome of weight at birth. One possible limitation concerning information about the occurrence of smoking among mothers was that this information was collected through the mother’s own statement which means that we had to trust this statement. The default attitude against patients should be that we trust their statements but sometimes this can be incorrect and therefore a possible error source that could have an impact on the results of this study and other studies.

A somewhat unexpected finding was regarding gender where a significant difference was seen between the groups which indicates that being born male leads to greater risk of being born SGAW. Male birth weight rather tends to be greater than female birth weight as Saenger et al states [1] but this does not serve as an explanation since we used weight z-scores were gender is taken into consideration [32]. Indications that male gender is associated with SGA have not been cited in previous studies. It is rather female gender that has been associated with IUGR, which contradicts the findings in this study [34]. This finding cloud maybe be due to faultiness in our statistical programme or errors during the input of information into the data file, since this was made
manually. Although, gender is either male or female the risk of errors during input should be minimal. It is difficult to state the cause of this finding or if it is simply a coincidence and we can only suggest that future research should focus on whether gender has an impact on SGA birth or not.

Maternal age at delivery and pre-pregnancy BMI was factors that in this study did not exhibit any significant difference between mothers giving birth to a SGA child and mothers giving birth to a AGA child. This finding contradicts previous findings were the two factors have had an impact on birth weight [1,14,18]. Inadequate gestational weight gain is also associated with low maternal age at delivery and low pre-pregnancy BMI and since this study shows a difference between gestational weight gain amongst mothers of SGA children vs. AGA children a difference in maternal age at delivery and pre-pregnancy BMI could have been assumed [21]. Age of the mother at 16 years and below is a risk factor for insufficient fetal growth and lower birth weight which would also been a cause to assuming that age of the mother would differ between the groups [1,14]. But since few mothers had an age below 16 years the results was probably not effected. From our results we can assume that maternal age has no significant impact on the risk of giving birth to a SGA child. For some cases the weight or length of the mother was missing and therefore BMI could not be calculated. Most often the missing weights are usually missed at the delivery ward. Reason to why this information was missing is probably because of difficulty to get weighed at the delivery ward due to lack of time or strength of the mother. Other reasons could be that the mothers did not want to get weighed or measured, maybe because of overweight, and therefore important and deviant information might be missing. This could be the reason to why information concerning weight is missing at registration at maternal health care.

There are several different ways to define SGA, which in turn leads to that different subjects can be classified as SGA [1]. This is a problem when comparing studies internationally since different results can be seen, not because true differences in the population or medical care but rather because different subjects are compared. This is a problem that should probably be lesser of a problem if an international definition was introduced which would lead to comparisons between a more homologous groups of patients.

Determining type of analysis test in SPSS depends in some cases on whether the study population is normally distributed or not. Since the study population in this study was large it was sometimes difficult to determine whether a variable had a normal distribution or not since the tests for
normality included in SPSS, like Kolmogorov-S, often shows a false low P-value with increasing sample size. Therefore determination of normality was performed with the help of graphical examination and calculation of means and medians. The interpretation of the graphical examination is subjective and in cases were there is a subtle difference whether distribution is non-normal or normal, cases that are non normally distributed can be estimated as normally distributed and vice versa. Although with the help from comparing median and mean the evaluating of normality should be correct. Most of our p-values were very low (p = < 0.001) which reduces the risk for incorrectly rejecting the null-hypothesis.

Strengths of this study are the large sample size. Even though several subjects fell out because not meeting the criteria for SGA or AGA concerning weight this study can because of the large sample size be more or less reflect the content of the total placenta biobank. On the other hand, a large sample size gives to a greater extent room for the human error since all the information in the data set is inserted manually. Another strength is that information gathered from medical records was registered in forms which minimizes the room for a subjective assessment. At the same time using forms sometimes restricts assessments and important information that has no specific place in the form may be left out from the form and instead written in running text in the records from where we did not gather any information for this study. Furthermore, patients were asked if they agreed to being included in the placenta biobank why not all births during 2004 and 2012 at the Delivery ward at Örebro university Hospital are included in the analyses. Further strengths of this study is the numerous previous studies made concerning this subject and thereby the availability to compare this study to these and to see whether this study is concordant or if it in some way contradicts these previous findings. Since the majority of our findings are concordant we can assume the power of this study to be high. Our contradicting findings can either be due to that our results are in some way faulty or that the finding is locally deviant. In either way, further research is encouraged if there is a contradicting finding.

Unfortunately all the data in the sample collection could not be used. The years 2004 to 2007 needed to be supplemented and this meant withdraw information from paper records, which is a consuming process. These paper records also needed extraction from the archive which made the process even more lingering. Because of these limitations only 395 journals out of 1014 from year 2007 was completed and the remaining 3,998 subjects from year 2004 to 2007 could not be used. The loss of subjects is a limitation in this study since if all the subjects were to be completed this would have assumingly given a more precise picture of the characteristics among the SGA children
in the sample collection. Although it is questionable if the extra three and a half years would have had mattered since the frequency of SGA children has not changed during these years (table 3).

Likewise, z-scores for lengths were missing for the years 2004-2007. The reason for this is that calculation of z-scores takes time and during this study the time was to short. If z-scores for length had been available for all years, comparisons between children born SGA for weight and children born SGA for length would have been possible, as well as children born both SGA for weight and for length. Such comparisons may have given some indications on whether the SGA for weight child has the same or different characteristics as the SGA for length child, which many of the other studies regarding SGA children demonstrates. For example, the incidence is higher for SGA length children than for SGA weight children [5] and insufficient gestational weight gain has larger impact on weight than height for the newborn infant [1].

Furthermore, because z-scores of birth length were missing for the year 2007 even though birth length was a variable that was supplemented in this study, no AGA subjects born in 2007 was included in the analyses since the definition of AGA used in the study included having a z-score between -1.99 and 1.99 for length. This is a limitation since 695 subjects (10.7% of the AGA population) was ruled out, although it is questionable again whether this has a significant impact on our results.

**Conclusion**

The SGA children in this study show similar characteristics as SGA children described in previous studies. However, in disagreement with previous studies, we found that maternal age at delivery and pre-pregnancy BMI did not differ between the SGA children and the AGA children. We also found that being born male is more frequent among the SGA children, which has not been stated in previous studies. Further research is needed concerning these factors. We recommend a larger number of pre-pregnancy BMI being collected of the mothers to SGA children and to look into whether gender has an impact on being born SGA or not.
References


