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# Do placental lesions among term small for gestational age newborns differ according to the clinical presentation?



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#### ARTICLE INFO

ABSTRACT

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Keywords: Fetal growth restriction Hypertension Oligohydramnios Placental histopathological lesions Small for gestational age *Objective:* To examine the incidence of placental lesions among women who delivered isolated small for gestational age newborns (isolated-SGA) at term compared to placentas from non-isolated-SGA born at term, early SGA and appropriate for age newborns (AGA). *Study design:* A case–control study conducted at a university teaching hospital. Placentas of women who

delivered a newborn with a birthweight less than the 10th percentile were included. Group A (study group): isolated-SGA delivered at term. Group B (1st control group): Term SGA accompanied antepartum with oligohydramnios or maternal hypertension (non-isolated-SGA). Group C (2nd control group): early SGA delivered before 34 weeks. Group D (3rd control group): placentas of low risk women who delivered AGA newborns at term. A total of 307 placentas were included: 72, 81, 60 and 94 placentas from Groups A, B, C, and D respectively. The primary outcome was the incidence of placental lesions that characterize SGA.

*Results:* The most frequent placental lesion found among all groups was maternal obstructive lesions, which appeared in 45.8% and 45.7% of placentas from groups A and B respectively (p = 0.98). The incidence among group A was significantly higher than in group D (20.2%) (p = 0.0006) and lower than in group C (76.7%) (p = 0.0004). The incidence of any placental lesion that characterized SGA among group A (69.4%) was 7.9 times higher than in group D (22.3%) (p < 0.0001) and comparable to group B (61.7%) (p = 0.3). The incidence of any placental lesion was highest among group C (83.3%).

*Conclusions:* The incidence of placental lesions was comparable among term SGA regardless of whether isolated or not and significantly higher than among AGA newborns.

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#### 1. Introduction

Fetal growth restriction (FGR) is defined as antepartum estimated fetal weight less than the 10th percentile for gestational age, and small for gestational age (SGA) is defined as newborns delivered with a birthweight less than the 10th percentile, according to the recent American College of Obstetrics and Gynecology (ACOG) practice bulletin [1]. FGR places the fetus and newborn at risk for morbidity and mortality in the perinatal period and predisposes the child to a lifelong increased risk for cardiovascular renal and metabolic disorders [2–4]. Concerns about intrauterine demise as opposed to the consequences of labor induction and timing of delivery are some of the debates that exist when managing these cases. Several studies have reported that

\* Corresponding author at: Department of Obstetrics and Gynecology, Emek Medical Center, Afula 18101, Israel. Tel.: +972 4 6494031; fax: +972 4 8141533. *E-mail addresses*: salim\_ra@clalit.org.il, raed\_s@bezeqint.net (R. Salim). placental histopathological lesions are present in 55% to 66% of women who delivered SGA newborns compared to about 30% from placentas of newborns delivered appropriate for gestational age [5–7].

Most of these studies, however, do not distinguish between the placenta-related findings and the accompanying clinical presentation and therefore do not provide clues that may assist clinicians in selecting the appropriate management in those situations. Egbor et al. reported that late onset FGR, either in isolation or in coexisting with preeclampsia, was associated with abnormal villous and vascular morphology, but there was no mention of whether oligohydramnios was accompanied or not [8].

While it is accepted to offer induction to women with FGR accompanied with oligohydramnios or hypertension diagnosed near or at term, there is no consensus in the management of isolated FGR at term. We aimed in this study to examine the extent of placental lesions among normotensive women who delivered isolated SGA newborns at term. Following the ACOG recommendation [1], the term "SGA" newborns will be used in this study to

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describe the study group and the controls who were delivered with a birthweight less than the 10th percentile for gestational age. "FGR" when used will refer to fetuses with an antepartum estimated fetal weight less than the 10th percentile for gestational age [1].

#### 2. Material and methods

This was a case–control study that included women who delivered SGA newborns defined as a birthweight less than the 10th percentile according to Israeli charts [9], between January 2007 and June 2011. Women who did not undergo an ultrasound examination for amniotic fluid index before delivery, had missing data regarding blood pressure measurements, uncertain dating, antepartum diagnosis of fetal structural or chromosomal abnormalities and multiple gestations were excluded.

Placentas from eligible women were divided into three groups. Group A (the study group) included placentas from normotensive women who delivered at term (37-41 completed weeks) newborns with a birthweight less than the 10th percentile. Fetal assessment before delivery revealed a normal amniotic fluid index and normal umbilical artery Doppler studies in cases where FGR was diagnosed antenatally. Women who developed postpartum hypertension until discharge were excluded from this group. Group B (first control group) included placentas from women who delivered at term newborns with a birthweight less than the 10th percentile and had a hypertensive disorder antepartum or postpartum while in the hospital, or oligohydramnios defined as amniotic fluid index less than 5 cm that developed or was diagnosed antepartum at term. Group C (second control group) included placentas from women who delivered newborns with a birthweight less than the 10th percentile before 34 weeks due to either maternal or fetal indications. These indications included, besides the antepartum diagnosis of early FGR, early severe preeclampsia, placental abruption, oligohydramnios or reverse or absent end diastolic flow measured at the umbilical artery accompanied with nonreassuring fetal heart rate tracing or due to intrauterine fetal death. Group D (third control group) included placentas from healthy low risk women who had uneventful pregnancies and delivered either spontaneously or by an elective cesarean at term, newborns with a birthweight that was appropriate for gestational age. Placentas from this group were consecutively collected from eligible women after the local Institutional Review Board approval and each woman from this group only, signed an informed consent since recruitment of this group only was made prospectively.

Mild and severe preeclampsia were defined according to the criteria published by the Society for Maternal-Fetal Medicine [10]. Doppler studies of the umbilical artery were not regularly performed in cases where FGR was not suspected before delivery, among women admitted in labor and in cases where delivery was indicated regardless of the Doppler study results.

Relevant demographic and obstetric characteristics were extracted from the electronic medical records at admission, electronic labor charts and medical records at discharge. The local Institutional Review Board approved the study.

Placental pathologic examinations were performed according to a standard protocol. All placentas were formalin fixed after trimming of the cord and the membranes and the placental trimmed weight was recorded. Histological samples were taken to include eight to ten blocks of placenta which comprised the full thickness of the placenta, extending from the fetal to the maternal surface, including both amnion and decidua. Sections were taken randomly from the central region in cases where no local lesions were macroscopically apparent. Blocks and slides from the placenta were submitted for review by the same pathologist (M.O.), who was blinded to the group allocation. Placental lesions which were considered in this study were those found to be significantly increased among pregnancies complicated by SGA newborns [7]. These included maternal obstructive lesions (increased syncytial knots, intervillous fibrin and villous infarct), fetal vascular obstructive lesions (fetal thrombotic vasculopathy and avascular villi), villitis of unknown etiology and perivillous fibrinoid deposition. The presence of infarct was determined when diameter was macroscopically greater than 3 cm or in the presence of infarcts in more than 25% of the dissection area. Microscopically, the presence of lesions was determined when they appeared extensively in the majority of the slides.

The present study aimed to compare between the incidences of placental lesions among the study group (isolated SGA) to that found among placentas from the control groups. Redline [7] reported that maternal vascular obstructive lesions were the most frequent placental finding among SGA and were present in 47% of the placentas of SGA newborns as compared to 20% among placentas of women who delivered appropriate for gestational age newborns. Accordingly, a sample size of 54 women in each group was sufficient in order to show a difference of 27% between the study group and group D with an alpha of 0.05 and a power of 80% (while 70 women in each group were sufficient to show the same difference with an alpha of 0.05 and a power of 90%).

Dependence between the groups' variables and other categorical variables was analyzed using the  $\chi^2$  test or Fisher's exact test (where 20% or more of the cells in a  $\chi^2$  table had an expected count of less than 5). For continuous data, differences between the four groups (A. B. C and D) were assessed using ANOVA or the Kruskal-Wallis test when the data were not normally distributed. To account for multiple testing, we used the Bonferroni correction which we considered significant only when test results presented p < 0.05/6 = 0.0083 when all four groups were analyzed and p < 0.05/3 = 0.0167 when the analysis did not include group D. Univariate and multiple logistic regressions were applied to assess which variables influence the probability of having any lesion. The Cochran-Armitage trend test was used to test whether lesion frequencies increase with lower percentiles. Statistical analyses were carried out using SAS 9.2 for Windows. Significance was set at *p* < 0.05.

#### 3. Results

A total of 213 eligible placentas from SGA newborns were included in this study: 72, 81 and 60 placentas met the inclusion criteria of groups A, B and C respectively.

Seventy-eight placentas from singleton SGA newborns were excluded due to missing data on admission or uncertain dating, or due to antepartum diagnosis of fetal structural or chromosomal abnormalities. Group D consisted of 94 placentas that met the inclusion criteria. Maternal characteristics of the four groups are presented in Table 1. The incidence of women who had maternal serum alpha fetoprotein (MSAFP) and/or human chorionic gonadotropin (HCG) above 2.0 multiples of the median in the second trimester was comparable between groups A and B and significantly lower than group C. Women in group D had normal biochemical screening as a prerequisite inclusion criterion and accordingly were not included into the statistical calculation. Perinatal outcomes are presented in Table 2.

Mean placental weight did not differ significantly between groups A and B whereas comparisons with groups C and D were significantly different (Table 3). The most frequent placental lesions found among all groups were maternal vascular obstructive lesions (Table 3). For women in group A, the odds of having any maternal vascular obstructive lesion were 3.3 times higher than for women in group D (p = 0.0006; OR 3.3; 95%CI 1.7–6.6). There were Download English Version:

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