Intrauterine growth restriction. Department experience and literature review

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Abstract

Objectives. *Evaluation of activity and experience of the Department of Obstetrics and Gynecology, Bucharest Emergency University Hospital and a systematic review of literature.* ***Methods.*** *We analyzed the incidence and distribution of Apgar scores at 1 and 5 minutes depending on gestational age and birth weight in 1419 patients with single pregnancies that gave birth between 01.01.2007 - 31.12.2012 in our department diagnosed with intrauterine growth restriction of at least 3 weeks.* ***Results.*** *Mean Apgar score at 1 minute was 8.63 ± 0.892 and 9.16 ± 0.674 at 5 minutes. Mean gestational age was 37.92 ± 1.246 weeks. Asymmetric intrauterine growth restriction was more frequent among these patients.* ***Conclusions.*** *Although the number of patients was significant, due to small variations, the results have not reached conventional statistical significance.*

Keywords: *intrauterine growth restriction, Apgar score*

Introduction

Intrauterine growth restriction (IUGR) is an important public health problem in both industrialized countries and developing countries, leading to perinatal long or short term morbidity and increased mortality. Of greater importance is the correct identification of IUGR, as the small weight of the newborn at birth determines specific conduct surveillance and antenatal and postnatal care[(1)].

Intrauterine growth restriction (IUGR) is defined in the most recent studies as the fetus unable to reach its genetic growth potential and it is considered to be the newborn with a birth weight below the 10th percentile or above two standard deviations (SD) below the average gestational age feature. It is often used as a synonym for newborn small for gestational age (small for gestational age-SGA)[(2)].

Recently the survival rate of children with IUGR increased, imposing further development of methods and means of investigating the health of the newborn, extending equipment and function monitoring systems to during childhood, adolescence and even adulthood[(3)].

Moreover, improved technology allowing recognition of both the cause and consequence, clarified that SGA and IUGR are not synonymous and that in itself is not a pathological condition, but only indicates an increased risk of adverse perinatal development as a result of a disease: maternal, fetal or placental[(4)].

Equally true is the fact that modern methods of prenatal diagnosis are frequently used in obstetrics and gynecology services in developed countries or in large medical centers in developing countries and as a result, the diagnosis is often established after birth.

Methods

There were evaluated data of all patients who gave birth between 1 January 2007 - 31 December 2012 or 27,462 patients Obstetrics and Gynecology Clinic Bucharest Emergency University Hospital. Inclusion criteria were the diagnosis of intrauterine growth restriction over three weeks without taking into account the generating cause. Twins or triplets were excluded. Intrauterine growth restriction was defined as fetal weight below the tenth percentile the. Data were obtained from observation charts of patients and newborns.

Statistical analysis was performed using SPSS version 19 and Microsoft Excel.

The variables included in the study were gestational age, birth weight and Apgar score at 1 minute and 5 minutes and statistical diagnosis (diagnosis).

We used descriptive analysis (mean, median, maximum, minimum, standard deviation, variance) and Crosstabulation for checking Apgar score frequency among patients with low weight and small gestational age.

Results

From all patients who were born between 1 January 2007 - 31 December 2012 were included in the study 1419.

The analyzed sample of 1419 showed that 74.5% of the cases had the diagnosis of asymmetric intrauterine growth restriction and the remaining 25.5% was symmetrical (Table 1).

Statistical analysis shows that the mean gestational age was 37.92 ± 1.246 weeks. 50% of cases had a gestational age less than 38 weeks and 75% of cases had a gestational age less than 39 weeks. The rest had gestational age less than 37 weeks (Table 2).

Distribution of births by gestational age shows that the highest frequency of 36.6% (520/1419) of births was among those with a gestational age of 38 weeks (Table 3).

In terms of birth weight newborns had an average weight of 2619.23 ± 217.53 g (1600 and 4000g) (Tables 4 and 5).

Mean Apgar score at 1 minute was 8.63 ± 0.892 and 9.16 ± 0.674 5 minutes (Tables 5 and 6). About 66% of cases had an Apgar score of 9 at 1 minute and 66% and 60.3%

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Table 1 Frequency of intrauterine growth restriction in the selected group

Diagnostic		Frequency	Percent	Cumulative Percent
Valid	Low weight for GA	1057	74,5	74,5
	Low height for GA	362	25,5	100,0
	Total	1419	100,0	

Table 2 Frequency of gestational age in selected group

N	Valid	1419
	Missing	0
Mean		37,92
Std. Deviation		1,246
Minimum		32,00
Maximum		42,00
Percentiles	25	37,00
	50	38,00
	75	39,00

Table 3 Distribution of births by gestational age

Gestational age		Frequency	Percent	Cumulative Percent
Valid	32,00	1	,1	,1
	33,00	3	,2	,3
	34,00	15	1,1	1,3
	35,00	28	2,0	3,3
	36,00	91	6,4	9,7
	37,00	332	23,4	33,1
	38,00	520	36,6	69,8
	39,00	311	21,9	91,7
	40,00	96	6,8	98,4
	41,00	19	1,3	99,8
	42,00	3	,2	100,0
	Total	1419	100,0	

Table 4 Description of selected group by weight at birth

	N	Minimum	Maximum	Mean	Std. Deviation
Weight	1419	1600,00	4000,00	2619,23	217,532
Valid N (listwise)	1419				

Table 5 Distribution of selected group weight

N	Valid	1419
	Missing	0
Percentiles	25	2500,00
	50	2650,00
	75	2750,00

had a 5-minute Apgar score of 9. We found an increase in values from 1 minute Apgar scores at 5 minutes for each group (Tables 7 and 8).

In order to see if there is a correlation between Apgar score at 5 minutes and birth weight, we grouped our patients in 4 weight classes:

Group 1 if weight <= 2400 g, Group 2 if weight is 2400-2600 g, Group 3 if weight is 2600-2800 g and Group 4 if weight> 2800g.

Table 6 Apgar score at 1 and 5 minutes, respectively

	N	Minimum	Maximum	Mean	Std. Deviation
Apgar score at 1 minute	1419	1,00	10,00	8,63	,892
Apgar score at 5minutes	1419	5,00	10,00	9,16	,674
Valid N (listwise)	1419				

Table 7 Apgar score with valid and missing numbers

		Apgar 1	Apgar 5
N	Valid	1419	1419
	Missing	0	0
Percentiles	25	8,00	9,00
	50	9,00	9,00
	75	9,00	10,00

Table 8 Frequency of the 1-minute Apgar score in the selected group

Calculated Apgar score after 1 minute		Frequency	Percent	Cumulative Percent
Valid	1,00	3	0,2	0,2
	2,00	2	0,1	0,4
	3,00	3	0,2	0,6
	4,00	2	0,1	0,7
	5,00	5	0,4	1,1
	6,00	15	1,1	2,1
	7,00	69	4,9	7,0
	8,00	313	22,1	29,0
	9,00	942	66,4	95,4
	10,00	65	4,6	100,0
	Total	1419	100,0	

Table 9 Frequency of the 5-minute Apgar score in the selected group

Calculated Apgar score after 5 minutes		Frequency	Percent	Cumulative Percent
Valid	5,00	2	0,1	0,1
	6,00	4	0,3	0,4
	7,00	20	1,4	1,8
	8,00	119	8,4	10,2
	9,00	856	60,3	70,5
	10,00	418	29,5	100,0
	Total	1419	100,0	

Unfortunately, the sample provides little information since most cases are the values of Apgar score above 8. We expected that the group with high score weight values prevail in categories 3 and 4. It is noted that in all infants with score 8, 10.9% are in Group 4 weight. This percentage is higher for those with score 10 (16.7%). It also states that the percentage of cases classified in Group 1 weight score decreased from 8 (27.7%) to score 10 (11%) (Table 9).

We tried to verify the correlation between gestational age and Apgar score at 5 minutes by dividing the patients according to gestational age into four groups.

Group 1 for VG <= 36 weeks, Group 2 for VG = 37 weeks, Group 3 for VG = 38 weeks and Group 4 for VG> = 39 weeks.

It appears that most of the Group 1 had an Apgar score of 9 (89/1419). As expected, there was an increase of Apgar score with the increasing gestational age (Tables 10 and 11).

Table 10 Distribution of Apgar score by weight in the selected groups Crosstabulation

Calculated Apgar score after 5 minutes		Groups by weight				Total
		1,00	2,00	3,00	4,00	
5,00	Count	0	1	1	0	2
	% within Apgar5	0,0%	50,0%	50,0%	0,0%	100,0%
6,00	Count	1	1	2	0	4
	% within Apgar5	25,0%	25,0%	50,0%	0,0%	100,0%
7,00	Count	4	8	5	3	20
	% within Apgar5	20,0%	40,0%	25,0%	15,0%	100,0%
8,00	Count	33	30	43	13	119
	% within Apgar5	27,7%	25,2%	36,1%	10,9%	100,0%
9,00	Count	144	256	376	80	856
	% within Apgar5	16,8%	29,9%	43,9%	9,3%	100,0%
10,00	Count	46	101	201	70	418
	% within Apgar5	11,0%	24,2%	48,1%	16,7%	100,0%
Total	Count	228	397	628	166	1419
	% within Apgar5	16,1%	28,0%	44,3%	11,7%	100,0%

Table 11 Distribution of Apgar score by age (Crosstabulation)

		Groups by age				Total
		1,00	2,00	3,00	4,00	
5,00	Count	0	1	1	0	2
	% within Apgar5	0,0%	50,0%	50,0%	0,0%	100,0%
6,00	Count	0	1	1	2	4
	% within Apgar5	0,0%	25,0%	25,0%	50,0%	100,0%
7,00	Count	10	6	1	3	20
	% within Apgar5	50,0%	30,0%	5,0%	15,0%	100,0%
8,00	Count	20	29	35	35	119
	% within Apgar5	16,8%	24,4%	29,4%	29,4%	100,0%
9,00	Count	89	211	325	231	856
	% within Apgar5	10,4%	24,6%	38,0%	27,0%	100,0%
10,00	Count	19	84	157	158	418
	% within Apgar5	4,5%	20,1%	37,6%	37,8%	100,0%
Total	Count	138	332	520	429	1419
	% within Apgar5	9,7%	23,4%	36,6%	30,2%	100,0%

Discussion

Intrauterine growth restriction (IUGR) is an important public health problem in both developing countries and industrialized countries, leading to diverse perinatal morbidities. 50% of neonates with IUGR associate a significantly increased adverse outcome, short or long term morbidity (meconium aspiration pneumonia, abnormal neurological development,

heart disease, hypertension, hypoglycemia, hypocalcaemia, type 2 diabetes) and an increased mortality of 6 to 10 times[1] and it has been postulated that also some diseases (cardiovascular and metabolic) present in adult life can be the consequence of in utero deprivation[2].

IUGR prevalence in the general population is about 8% and there is evidence to support the fact that 10% of perinatal mortality is a consequence of IUGR[3]. It has been shown that IUGR is associated with up to 52% of stillbirths[4] and that SGA below the 10th percentile are associated with up to 72% of unexplained fetal deaths[5].

The World Health Organization considers SGA to be defined as a birth weight lower than 2500 grams for a term newborn[6], thus eliminating the impact of accurate pregnancy dating and allowing other developing countries to use this definition. Still, an estimated weight below the 10th percentile for gestational age or weight that is less than two SD below the anticipated value for the gestational age in has been adopted and used with more ease. However, if the limit definition is corroborated below the 5th percentile or below 2 SD only 3-5% of all pregnancies will enter in this category, the ones that are actually growth restriction (IUGR) pregnancies due to chronic fetal distress and risk[7].

Although IUGR etiology is diverse, stakeholders can be grouped into four categories: maternal, placental, fetal and idiopathic. Maternal factors are represented by: multiple pregnancy, maternal malnutrition, decreased uteroplacental blood flow, drug use, consumption of anticancer chemotherapy drugs, corticosteroids, cyclosporine and antihypertensives[8], maternal hypoxia, extreme ages, thrombophilia, hypoplasia of uterus, other as ethnicity or race, socioeconomic status, maternal education, history of previous pregnancies (abortions, previous premature births, babies with IUGR before, first pregnancy, multiparity) mother's medical history, medical complications of pregnancy, body mass index and weight gain during pregnancy, timing and number of prenatal visits[9] and maternal size.

Placental conditions represent the most frequent etiology of IUGR: placental insufficiency, anatomical abnormalities, others like corioamniotitis, hemangiomas, placental tumors, single umbilical artery, *abruptio placentae*, *placenta praevia*. Fetal factors are genetic, chromosomal birth defects, cardiovascular abnormalities, congenital infections, metabolic diseases. Idiopathic factors determined from a third to a quarter of newborns with IUGR[10].

The cornerstones of management for the pregnancy complicated by IUGR are surveillance of fetal growth velocity and homeostasis and determination of appropriate delivery timing. If fetal growth has continued to be adequate and antenatal testing results have been normal, delivery at or near term is usually indicated. Management is far more challenging remote from term and requires use of the biophysical profile (BPP), measurement of amniotic fluid volume (AFV), and Doppler assessment of the fetal circulation, combined with good clinical judgment. There are no efficient methods for preventing IUGR, not simple means anyway because of the multifactorial nature of the condition. There is evidence that suggests that perinatal outcome may be improved by optimizing the timing of the delivery and by preventing the adverse consequences after the diagnosis of IUGR[11].

Some of the methods used to predict and monitor growth of the fetus include maternal BMI screening which had been proposed as an effective method of predicting fetal growth by a group of experts[12,13], pubis-fundal height measurement and routine ultrasound[12].

No effect in reducing perinatal mortality had been shown by two Cochrane reviews on routine ultrasound evaluation in late (after 24 weeks of gestation) as well as early pregnancy (before 24 weeks of gestation)[14,15].

Ultrasound performed in early pregnancy was however beneficial in reducing rates of induction of labor for post-term pregnancies and in detecting multiple pregnancies[15].

However, ultrasound examination gives us the opportunity to effectively classify the restricted fetuses growth, based on their volume (less than 5%), based on slow growth of abdominal circumference, sluggish LA, and by the presence of abnormal Doppler umbilical artery (artery and uterine) spectra.

Another Cochrane review on effectiveness of pubis-fundal height measurement was inconclusive as only one trial was included and no recommendations in favor or against of the intervention were made[16].

An ideal way to classify abnormal fetal growth is by taking into consideration not just the fetal weight, which is known to be a good indicator of increase of morbidity and mortality[17], but also other indicators of fetal and placental normal development in order to enhance the accuracy of defining IUGR.

Antenatal testing modalities for fetal health, including analyzing the fetal heart rate, assessing amniotic fluid volume, biophysical profile and evaluating Doppler fetal and maternal vessels and for placental function, are the most common clinical tools that are used[18].

This was also concluded and supported by another study that stated that SGA fetuses with normal Doppler studies are most likely constitutionally small, as they showed no increase in morbidity rates and not pathologically growth-restricted fetuses compared with average for gestation fetuses[19].

Abnormal levels of different maternal serum markers have been shown to be associated with growth restriction and poor placental function and Down

syndrome[20] such as alpha-fetoprotein, pregnancy-associated plasma protein A, human chorionic gonadotrophin, oestriol, inhibin A and activin A[21].

Recently, a number of studies have found a significantly association between angiogenic and anti-angiogenic factors (vascular endothelial growth factor, placenta growth factor, soluble vascular endothelial growth factor receptor-1 and soluble endoglin) and early-onset growth restriction[22,23,24].

However, since the previous studies focused mainly on predicting pregnancy complications as early as possible during pregnancy, more research is needed in order to evaluate the usefulness of these biomarkers as indicators of placental function in late pregnancy and as clinical specificity and sensitivity.

Although still limited, literature regarding genetic epidemiology is increasing in evidence suggesting that fetal growth might be associated with genetic variations. Of specific interest are the genes coding for Insulin-like growth factors I and II, Insulin and their receptors. If proven valid, they could provide a significant improvement of the predictive ability of screening and diagnostic tests aimed at investigating fetal growth[25].

In summary, the growth potential of the fetus, current fetal size, fetal and placental health, and, if available, fetal growth velocity should be taken into account in order to obtain a good definition for IUGR.

However, as IUGR has a multifactorial etiology[26] none of these factors alone seems to be able to discriminate with great certainty between constitutionally and pathologically small fetuses.

A promising concept appears to be an integrated diagnosis with multiple modalities but as many basic issues in assessing fetal growth have yet to be addressed it requires further development and testing.

To meet these basic needs, the National Institutes of Health in the U.S. and the World Health Organization have recently launched multi-country, multi-race/ ethnicity studies. An integrated definition building upon these findings could potentially be a useful tool to improve classification of whether or not a fetus is growth-restricted in various countries, races and ethnicities.

IUGR remains a serious multidisciplinary problem, due to the difficulties in identifying and monitoring these fetuses prenatal as well as postnatal and because of the increased perinatal mortality and morbidity associated.

Conclusions

Overall, we found no convincing new associations in our study between 1-minute and 5-minute Apgar score and gestational age and birth weight in our study group. But our study does emphases, through the rising values of the 1-minute Apgar score to 5-minute Apgar score that the fetuses outcome were favorable due to close monitoring and intervention if needed regarding the newborns and their mothers. Another important factor that contributed to the favorable outcome of both mother and newborn, is the close interdisciplinary collaboration between the obstetric-gynecology department, the neonatology department and the intensive care unit/ anesthesiology department. ■

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