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Intrauterine growth restriction: contemporary issues in diagnosis and management

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Abstract

Background: Intrauterine growth restriction represents a fetal life treating condition in obstetrics. Diagnosis and appropriate management during pregnancy is essential because of the considerable morbidity and mortality to which restricted new-borns are exposed. Implementation of diagnostic criteria could potentially determine an optimized outcome in these patients.
Material and methods: The article reflects a study of 728 cases of patients delivered to the Obstetrical department of Municipal Hospital No1, Chisinau, the Republic of Moldova during January-December 2016. A special protocol for clinical and paraclinical data collection was used. From these 728 cases, 50 histories of low birth weight fetuses (<2500g) were analysed in detail.
Results: The average weight of LBW fetuses was 2057 gr. 27 fetuses (54%) were diagnosed as intrauterine growth restricted fetuses. The average weight of fetuses with the diagnosis of IUGR was 1989 gr. 18.52% infants had a very low birth weight (1000-1499 g.), 84.48% infants had low birth weight (2500-1500 g).
Conclusions: The prevalent criteria for diagnosis of intrauterine growth restriction in our study were foetal abdominal circumference below 10th percentile (52.3 %). The ultrasound evaluation showed to have an average sensitivity in the predicting the foetal weight at birth (47.6%). In the majority of cases the delivery was done by cesarian section (62.9%), with the most frequent indication for foetal extraction – vascular redistribution and beginning of cerebral vasodilatation (37.5 %).

Key words: intrauterine growth restriction, small for gestational age, foetal Doppler, foetal biometry.

Introduction

Intrauterine growth restriction is a major public health problem both in the industrialized and developing countries. For obstetricians – gynaecologist's foetal intrauterine growth restriction means important risk for iatrogenic prematurity, foetal distress, impaired neurodevelopment, cerebral palsy and perinatal death [1]. The prognosis in neonatal intrauterine growth restriction depends on the severity of the etiological factors, presence of foetal prematurity, foetal distress, cerebral anoxia, perinatal asphyxia and meconium aspiration syndrome [2]. Diagnosis and appropriate management during pregnancy is essential because of the considerable morbidity and mortality to which restricted new-borns are exposed. Not to diagnose an intrauterine affected foetus means to jeopardize its vital prognosis. On the other hand, to deliver the foetus before term is to induce the risc of prematurity. The clinician is always measuring risk of delivery in very early gestation with associated morbidity against the risk of fetal death if the fetus remains in utero [3]. Conversely, to label a normal foetus by mistake as being growth restricted means to expose him to unnecessary interventions.

Thus, antenatal detection of intrauterine growth restriction and correct clinical management can improve outcome for these neonates. Also, we have to mention that till now, no evidence-based management protocols are available [4].

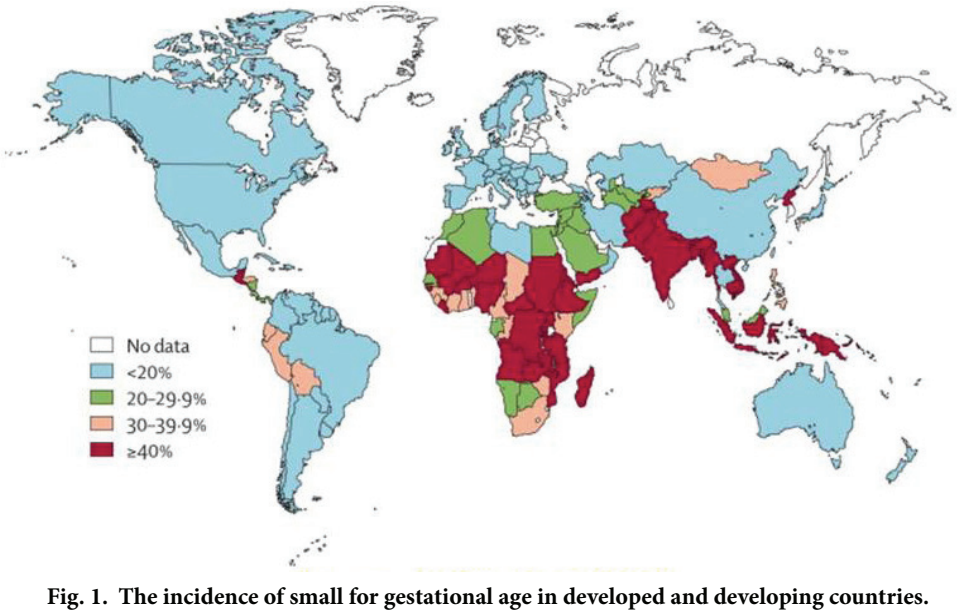

Fig. 1. The incidence of small for gestational age in developed and developing countries.

The Lancet in 2008 reported the incidence of foetal growth restriction in developed countries is 3-7% of birth, while in developing countries is up to 24-40% of cases [5] (fig.1).

In the Republic of Moldova the reported incidence is 6.3 ± 0.063% [6]. Normal fetal growth is determined by a number of factors. These include genetic potential, nutritional status of the mother, placental function and transfer of nutrients, and intrauterine hormones and growth factors. Numerous risk factors for foetal growth restriction have been described and classified into maternal, foetal and placental factors [7] (fig. 2).

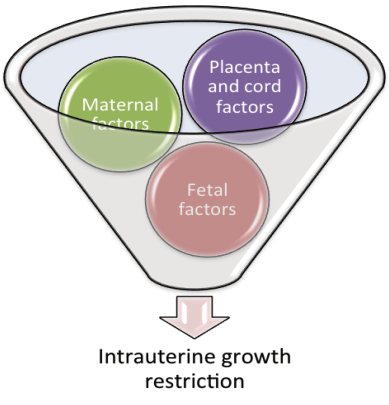

Fig. 2. Risk factors for fetal growth restriction.

Various maternal factors may lead to foetal growth restriction – under-nutrition hypertension, diabetes, anti-phospholipid syndrome, lupus erythematosus, hemoglobinopathies, maternal infections, chronic illness, drug abuse and drug exposure, smoking [8]. Foetal genetic syndromes and chromosomal disorders – trisomies 21, 13 and 18 and Turner's syndrome are associated with higher rates of growth restriction [9]. Placental and cord anomalies- membranous cord insertion, placenta praevia are associated with higher rates of foetal growth restriction. Among all causes, uteroplacental insufficiency is thought to be the major cause of intrauterine growth restriction [10]. The literature includes several confusing and controversial terms and definitions related to intrauterine growth restriction. There is no universally accepted definition of intrauterine growth restriction and most statistics include such terms as "small for gestational age", "low weight at birth", "very low weight at birth". These also include distinctions between 'references' used by the obstetricians, and those used by the paediatricians. In general, small for gestational age is defined as a birth weight below a certain limit compared with a population-based reference curve, while intrauterine growth restriction is defined as a failure to reach the genetic growth potential and always implies pathological growth [11]. For both "small for gestational age" and intrauterine growth restriction fundal height measurement is a screening method. This investigation has little ability to differentiate between normal but small fetus and the fetus at perinatal mortality and morbidity [12]. There are no universally accepted criteria for the diagnosis of abnormal foetal growth. Obstetrical literature as diagnostic criteria proposes: a) a fall in symphysis-fundus curve; b) deviation in ultrasound fetometry; c) pathological Doppler examination of the umbilical artery in small for gestational age fetus; d) pathological amniotic fluid volume in small for gestational age fetus [13]. The current gold standard for the diagnosis of abnormal foetal growth remains biometry: the most used definitions are based on abdominal circumference or calculated foetal weight for a given period of gestation below the 10th percentile [14]. Till now, there is no consensus on whether the diagnosis of intrauterine growth restriction, should be based on estimated foetal weight, estimated abdominal circumference or both [14, 15, 16].

Material and methods

The article reflects a descriptive, non-experimental study with a general group of 728 patients hospitalized during 2016 in the Obstetrical department of Municipal Hospital No 1, Chisinau, the Republic of Moldova. Methods of data collection in the study were based on extraction of medical documentation data from archive to complete the elaborated questionnaire for research. Statistical processing was performed using the program "Microsoft Office Excel 2010".

Results and discussion

From these 728 cases, 50 histories of low birth weight fetuses (<2500g) were analyzed in detail. The average weight of neonates was 2057 g. 27 fetuses (54%) were diagnosed as intrauterine growth restricted fetuses. RGOG Green-top guideline defines small–for–gestational age as an infant born with a birth weight less than the 10th centile. For these standards or personalized population centiles are used [17]. The smaller is the percentile weight of the fetus the higher is the probability to have a growth restriction. Untrauterine growth restriction is not synonymous with small for gestation. 50–70% of small–for–gestational age fetuses are constitutionally small, others "pathologically small" or growth restricted. Such infants were shown to be at increased risk for neonatal death [18, 19]. For example, the neonatal mortality rate of small for gestational age infants born at 38 weeks was 1 percent compared with 0.2 percent in those with appropriate birthweights [20].

The average weight of fetuses with the diagnosis of intrauterine growth restriction was 1989 g. 18.52% of infants had a very low birth weight (1000-1499 g). 84.48% of infants had low birth weight (2500-1500 g). In our study we did not have infants with extremely low birth weight (500-999 g).

Correct establishment of gestational age and determination of maternal risk factors improve the identification of small for gestational age with possible adverse pregnancy outcomes such as stillbirth, neonatal death, or low Apgar score [21, 22].

Risk factors as: maternal age, parity, maternal body mass index, mass weight gain during pregnancy, practice of exercise, diet, drug abuse, smoking, pregnancy interval, previous still-birth and pregnancy hypertension, diabetes, renal disease, antiphospholipidic syndrome, sex of the fetus, and complications of present pregnancy were included in the study protocol [23, 24].

The average age of mothers of children with IUGR was 29.07 years, the age ranged from 21 to 38 years. They were divided into 4 age groups: 21-25 years, 26-30 years, 31-35 and > 36 years. The majority of mothers belonged to the age group of 26-30 years (37.04%), 21-25 years old was 25.93%, 31-35 – 22.22% and> 36 years – 14.81%. It was found that the majority of mothers of children with IUGR were from the age group up to 30 years – 62.96%. Over 30 years were 37.04%. These mothers were also divided into 2 groups according to their social status: a housewife or a working woman. The group of housewives predominated: 56% versus 44% of employees. Parity of pregnancy of mothers ranged from 1 to 5. Mothers with the first pregnancy – 55.56%. The second pregnancy accounted for 29.63% of mothers, the third one - 7.41%, the fourth and fifth – 3.70%. By parity of birth, the mothers were divided into 3 groups: mothers with first birth made up the majority – 41.46%, second-birth – 29.27% and third birth were in 29.27%. Each of the examined risk factor has a likelihood ratio which can be used in calculation of general risk and particular antenatal management. This can include maternal serum markers in the first trimester of pregnancy, assessment of uterine Doppler, evaluation of the placenta morphology and serial ultrasound scans [25, 26].

Pregnancy-induced hypertension was diagnosed in 18.52%. Bad obstetric history was in 33.33% of pregnant women, 44.44% had scars on the uterus, 33.33% had miscarriage and 22.22% – infertility.

Gestational age was calculated using information from date of birth and estimated date of delivery determined in early pregnancy. The gestational age of children with IUGR was between 28 and 39 weeks. 28-32 weeks was 12.72%, 33-36 weeks – 43.80%, 37-39 weeks – 43.48%.

Normal fetal growth and development can be divided into three physiologic stages: cell replication and proliferation; cell migration and aggregation to form tissue and rudimentary organs; and increase in cell size and formation of functional organ structures. Thus in early pregnancy, very high mitotic activity is paired with very little change in mass, while in late pregnancy mitosis slows with a coincident rapid gain in weight [27]. As a result, genetic factors most influence fetal growth during the first half of pregnancy, and hormonal or environmental factors dominate later in pregnancy. Depending on this we can distinguish 2 different forms of intrauterine growth restriction: early and late [28]. These two forms are distinct by the cause, evolution, ultrasound parameters modifications, and postnatal outcome [29]. The diagnosis of intrauterine growth restriction in our study was mainly based on abdominal circumference value, with the prevalence of cases with 10th percentile abdominal circumference or linear growth chart. So the 10th percentile was used as a cut-off for hospitalization decision and fetal close monitoring [30].

The results of these ultrasound data (head circumference, abdominal circumference, femur length) were processed and compared to the percentile corridors: <3, 3-5, 5-10, >10. The difference between the estimated weight and the actual weight of the fetus was from 10 grams to 520 grams. The average difference was 255.71 grams. The difference <300 grams was 47.62%, > 300 grams was 52.38%.

The value of the head circumference of the fetuses in the majority was below the 10th percentile – 76.19%, head circumference >10 percentile – 23.81%, 5-10 percentiles – 9.52%, 3-5 percentiles – 33.33% and <3 percentiles were 33.33%. By the femur length most of the fetuses were found in the percentile > 10 (71.43%), 3-5 and 5-10 percentiles at 4.76% and in the percentile <3 were 19.05% of the fetuses. By the abdominal circumference most fetuses also belonged in corridor – the percentile 10 (52.38%), 3-5 and 5-10 percentiles at 4.76%, and <3 percentile – 38.10% (fig. 3). It was calculated for how many weeks the fetuses are lagging by the circumference of the abdomen from gestational age. Lagging by <2 weeks were 28.57%, for 2-4 weeks – 52.38%, for> 4 weeks – 19.05%. Fetal observation was based on fetal Doppler, amniotic fluid volume and cardiotocography [31, 32]. Of all the ultrasound results processed, 38.09% had pathological ombilical and middle cerebral artery Doppler (pulsativity index, resistance index and systolic/diastolic index). We used a Doppler follow-up program to distinguish various causes of small fetuses for gestational age. Small fetuses of small mothers and those small due to chromosomal aberration usually have normal Doppler tracings of umbilical and uterine arteries. The use of umbilical artery Doppler ultrasound has led to reductions in perinatal death related to complications of placental insufficiency and iatrogenic preterm delivery [33].

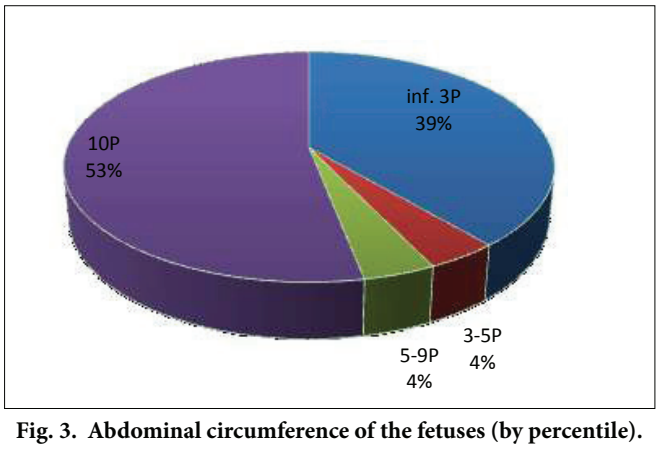

Fig. 3. Abdominal circumference of the fetuses (by percentile).

However, umbilical artery Doppler is not reliable for the identification of late-onset growth restriction and associated complications. Unfortunately, late-onset fetal growth restriction is more prevalent than growth restriction of early onset, and most adverse outcomes attributable to late-onset growth restriction occur in fetuses with normal umbilical artery Doppler waveforms [34].

Data of the circulation insufficiency, as data of blood circulation in the middle cerebral artery were in 38.09%. Of these, circulatory insufficiency was in 87.50% of cases. Most often there was a deficiency of I degree: 62.5% (IA-37.5%, IB – 25%). II degree of insufficiency – 12.5%, III degree – also 12.5%. Location of placenta was in 66.67% of cases anterior, 33.33% – posterior.

According to the delivery, 62.96% had a cesarean section, 37.04% had vaginal birth (fig. 4).

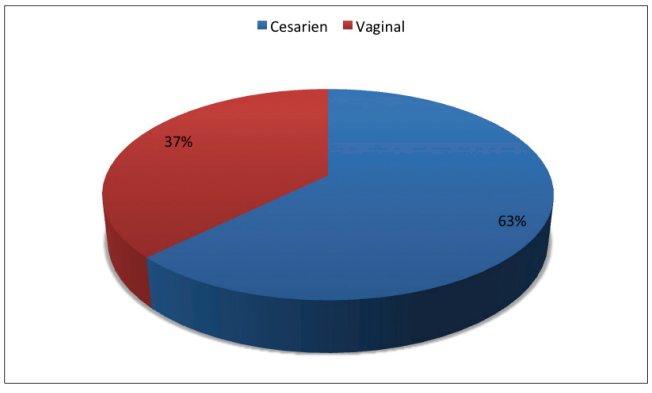

Fig. 4. Delivery modality of the fetuses.

As reported by Perroten et al., and Yogev et al. at least one half of all infants born with intrauterine growth restricted will experience intrapartum asphyxia at birth [35, 36]. Meconium aspiration and fetal hypoxia are also common [37]. Guidelines suggest that C-sections are more appropriate for infants with intrauterine growth restriction due to these risk factors and as mentioned earlier, due to their small size [14-16].

The female sex of newborns prevailed: 59.26%, male – 40.74%. We were also interested in Apgar score of the neonates, as in literature the antenatal detection and monitoring program for fetuses suspected with intrauterine growth restriction result in a better neonatal score, compared with cases of fetuses not identified antepartum [38].

The Apgar score at 1st minute for newborns with IUGR varied from 4 to 8. More children had score 7 (59.26%). Score 8 received 14.81% of infants, 4 – 3.70%, 5 and 6 points for 11.11% of newborns. The Apgar score at 5th minute – 7 points received 55.56% of children, 8 points – 33.33%, 5 points – 3.7%, 6 points – 7.41%.

Conclusions

The diagnosis and the management of intrauterine growth restriction still constitute a clinical dilemma. The prevalent criteria for diagnosis of intrauterine growth restriction in our study were foetal abdominal circumference below 10th percentile (52.3 %). The ultrasound evaluation showed to have an average sensitivity in the predicting the foetal weight at birth (47.6%). In the majority of cases the delivery was done by cesarian section (62.9 %), with the most frequent indication for foetal extraction – vascular redistribution and beginning of cerebral vasodilatation (37.5 %). Accurate diagnosis of intrauterine growth restriction can be achieved by improvement of methods for assessing the foetal biometry.

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