Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 2, 2012, pp. 225-233

EVALUATION OF RISK FACTORS INVOLVED IN INTRAUTERIN GROWTH RESTRICTION

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Abstract: The newborns with intrauterine growth restriction (IUGR) are a significant proportion, approximately 30% of infants with low birth weight (<2500gm). This paper aims to highlight the link between the existence of certain risk factors and intrauterine growth restriction, as well as specific neonatal pathology.
Keywords: intrauterine growth restriction, risk factors

INTRODUCTION

Of all newborns, approximately 7-10% has less than 2500 grams birth weigth, being called „newborns with low birth weight". Of these, two thirds are born prematurely (before 37 weeks gestation) and one thirds have a birth weight lower than that corresponding of their age of gestation, being called „small for gestational age" (SGA) or newborn with intrauterine growth delay or newborn hypotrophy [Taeusch et al, 2004]

To differentiate the two categories of newborns with low birth weight intrauterine growth, Usher and McLean, and respectively Lubchenco curves are used. Fetuses with growth retardation in these curves lie below 3 percentile in Usher and McLean curves and, below 10 percentile in Lubchenco curves [Lubchenco et al, 1963].

Newborns with intrauterine growth retardation (IUGR) fall into two categories [MacDonald et al., 2005]:

- Symmetric IUGR – Type I (early onset growth restriction – first trimester of pregnancy)
- Asymmetric IUGR – Type II (usually late onset growth restriction – second and third trimesters of pregnancy)

Differentiation of two types of growth retardation is important, because course of treatment and prognosis are different [Cunningham et al., 2005].

The main etiological mechanisms with effect of limiting the fetal growth potential are:

1. Intrinsic mechanisms (fetal factors) - these factors act in the first trimester of pregnancy, leading to a symmetrical growth restriction: genetic factors (racial, ethnic, sexual, and parental endowment), chromosomal diseases: (trisomies 21, 18, and 13 and many syndromes - Turner syndrome, X polisomy, dwarfism, chondrodystrophies, osteogenesis imperfecta), congenital anomalies - anomalies of almost any organ system can be associated with IUGR (CNS, gastrointestinal, renal abnormalities, pituitary growth hormone deficiency, hypothyroidism, metabolic disorders such as hypocalcaemia, hypyophosphatemia rickets, hypokalemia, galactosemia, glycogen storage disease, salt-losing congenital adrenal hyperplasia, cardiovascular abnormalities), congenital infection - such as TORCH infections, uterine crowding: multiple gestation, uterine abnormalities such as fibroids and bicornate uterus [American College of Obstetricians and Gynecologist. Practice Bulletin, 2000, Cloherty et al., 2010]

2. Extrinsic mechanisms (maternal and placental factors): these factors act in the second and third trimesters of pregnancy, leading to a asymmetric growth restriction.

- The maternal involved factors are: low socioeconomic status, poor maternal nutrition, substance abuse, teenage pregnancy, reduced uteroplacental blood flow - all may impair oxygen delivery and impair fetal growth (chronic hypertension, pre-eclampsia, chronic renal disease, collagen vascular disease, diabetes mellitus with vascular disease, congenital heart disease, hemoglobinapathies, uncontrolled hyperthyroidism with concomitant hypermetabolic state, sickle cell anemia), drugs (cigarettes, alcohol abuse, heroin/ cocaine/ methamphetamines and other ilicit drug use, use of other drugs or chemical agents such as antiepileptics, antimetabolites, steroids, and coumadin,) other maternal factors are short stature, young age, and multiparity [Cloherty et al., 2010, Cucken et al., 2002]
- The placental involved factors are: placental insufficiency (inadequate placental nutrients or blood supply to nourish the fetus), anatomic problems (aberrant cord insertion, thrombosis, placental involution and hemangioma) [Cloherty et al., 2010]

If intrauterine growth retardation is found, careful monitoring is needed to look for signs of fetal distress. There are several systems for monitoring fetal, all

using the same surveillance techniques: placental and fetal circulation assessment by Doppler velocimetrie and assessment of fetal well-being by nonstress test, contraction stress testing, oxytocin test, biophysical profile [American College of Obstetricians and Gynecologist - Education Pamphlet, 2002, Boito et al., 2004] .

If chronic intrauterine hypoxia is detected, optimal timing of birth are the focus of medical attitudes, the obstetrician being in a position to weigh the risk of prematurity and the risk of development of organic lesions [Williamset al., 2003, American Academy of Pediatrics – Textbook of Neonatal Resuscitation Book, 2007].

The birth of a fetus with intrauterine growth restriction is, in most cases, an obstetrical emergency, and the complications occurring in the neonatal period can be major: asphyxia at birth, meconium aspiration syndrome, hypothermia, persistent pulmonary hypertension, hypoglycemia, polycythemia, necrotizing enterocolitis, acute renal failure [Cloherty et al.,2010].

Long-term prognosis depends on the degree of damage to fetal and prematurity [Vergani et al., 2003].

MATERIALS AND METHODS

The study has been performed on a group of 411 of IUGR newborns of „Sf. Pantelimon" Hospital, Bucharest, from 1 October 2005 to 1 October 2010. The 411 SGA newborns represent approximately 39% of all newborns with low weight registered in the same maternity unit and covering the same period, respectively 1053 newborns. For that period, the total number of birth was 8775, with an average of 1755 per year. The diagnosis of growth restriction has been established on account of clinical aspect, position on the intrauterine growth curves and antepartum echographic data.

This has been a prospective method throughout neonatal period together with data collected on the evolution of the pregnancy.

The importances of the risk factors in growth restriction, the type of growth retardation and the complications throughout the neonatal period have also been analyzed.

RESULTS AND DISCUSSION

Of all 411 newborns with IUGR:

- 363 (88%) have been born on term
- 49 (12%) have been born prematurely

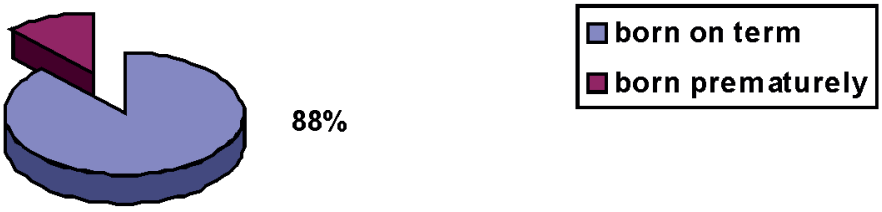

Figure 1. IUGR newborn: on term/premature

SGA term newborns:

● etiological factors involved:

►fetal factors (chromosomal anomalies, genetic syndromes, congenital malformations, multiple gestation, single umbilical artery, TORCH syndrome) – 51 (14%) cases

►maternal factors (low socioeconomic status, constitutional factors, Rrom (gipsy) ethnicity, extreme age, smoking, alcohol and drug use) – 261 (72%) cases

►placental factors (placental insufficiency) – 51 (14%) cases

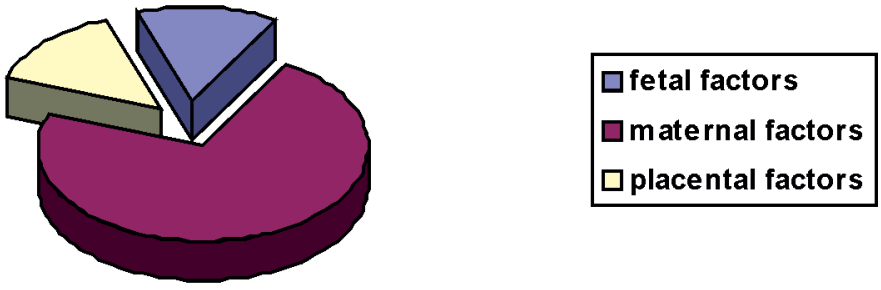

Figure 2. IUGR newborns on term: etiological factors

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 2, 2012, pp. 225-233

● based on therapeutic management through pregnancy: only 119 (33%) pregnancies have been supervised and the following methods have been used: standard ultrasound examination, placental and fetal circulation assessment by Doppler velocimetrie, biophysical fetal profile

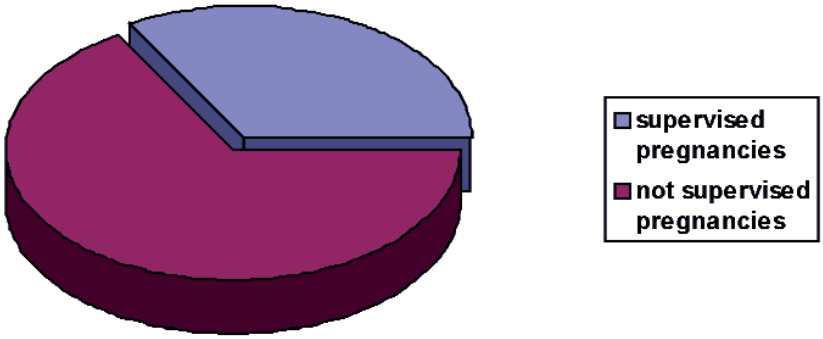

Figure 3. IUGR newborns on term: pregnancy management

● based on delivery management: in 62 (17%) cases caesarian sections have been performed

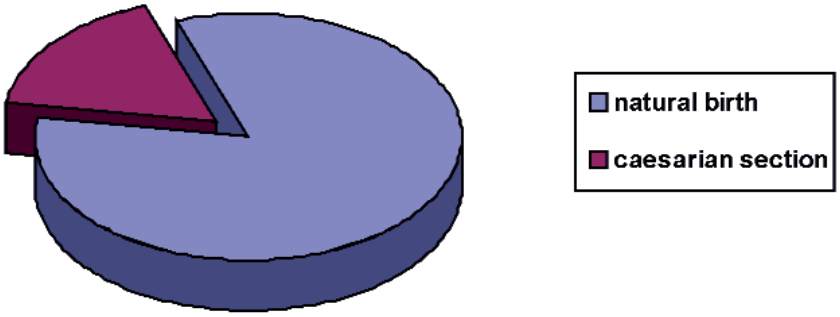

Figure 4. IUGR newborns on term: delivery management

● based on neonatal pathology, the following complications have appeared: perinatal asphyxia (Apgar score < 3) – 7 (2%) cases, persistent pulmonary hypertension (PPHT)– 5 (1,3%) cases, post asphyxia heart failure – 4 (1,1%) cases, acute renal failure – 3 (0,8%) cases, neonatal seizures – 20 (5,5%) cases, bleeding syndrome (disseminated intravascular coagulation, thrombocytopenia) – 23 (6,3%) cases, mild and moderate perinatal depression (Apgar score 5-7) – 60 (16,5%) cases, neonatal shock – 75 (19%) cases, hypothermia – 70 (19%) cases, polycythemia – 87 (24%) cases, transient neonatal hypoglycemia – 57 (15,7%) cases, neonatal hyperbilirubinemia – 53 (14,6%) cases

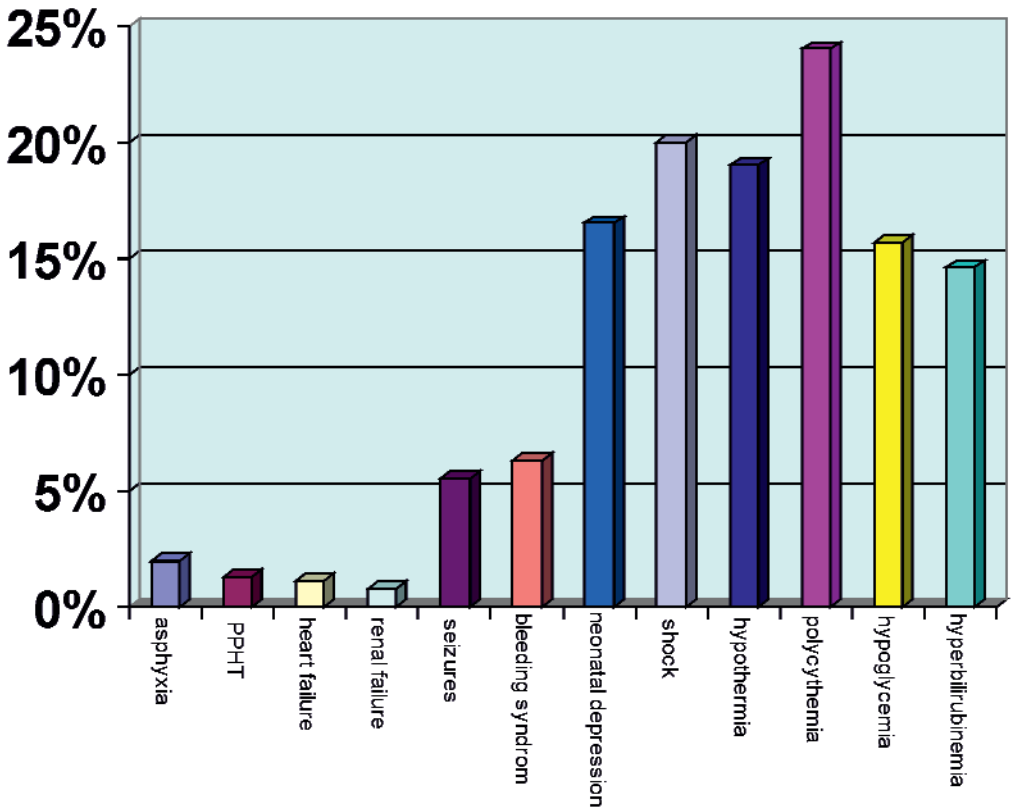

Figure 5. IUGR newborns on term: neonatal pathology

Neonatal complications related to etiological factors:

- perinatal asphyxia (7 cases) has only appeared in the cases with placental factors
- mild and moderate perinatal depression (60 cases) :45 cases (75%) – placental factors, 9 cases (15%) – fetal factors, 6 cases (10%) – maternal factors
- neonatal shock (75 cases): 59 cases (78,7%) – placental factors, 9 cases (12%) – fetal factors, 7 cases (9,3%) – maternal cases
- persistent pulmonary hypertension (5 cases) has only appeared in the cases with placental factors
- post asphyxia heart failure (4 cases) has only appeared in the cases with placental factors
- acute renal failure (3 cases) has only appeared in the cases with placental factors
- neonatal seizures (20cases): 10 cases (50%) – placental factors, 7 cases (35%) – fetal factors, 3 cases (15%) – maternal factors
- bleeding syndrome (23 cases): 13 cases (56,5%) – placental factors, 8 cases (34,8%) – fetal factors 2 cases (8,7%) – maternal factors
- neonatal hypothermia (70 cases): 47 cases (67,2%) – placental factors, 8 cases (11,4%) – fetal factors, 15 cases (21,4%) – maternal factors
- neonatal polycythemia (87 cases): 62 cases (71,3%) – placental factors, 10 cases (11,5%) – fetal factors, 15 cases (17,2%) – maternal factors
- transient neonatal hypoglycemia (57 cases): 43 cases (75,4%) – placental factors, 6 cases (10,6%) – fetal factors, 8 cases (2%) – maternal factors
- neonatal hyperbilirubinemia (53 cases): 25 cases (47,2%) – placental factors, 17 cases (32%) – fetal factors, 11 cases (20,8%) – maternal factors

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 2, 2012, pp. 225-233

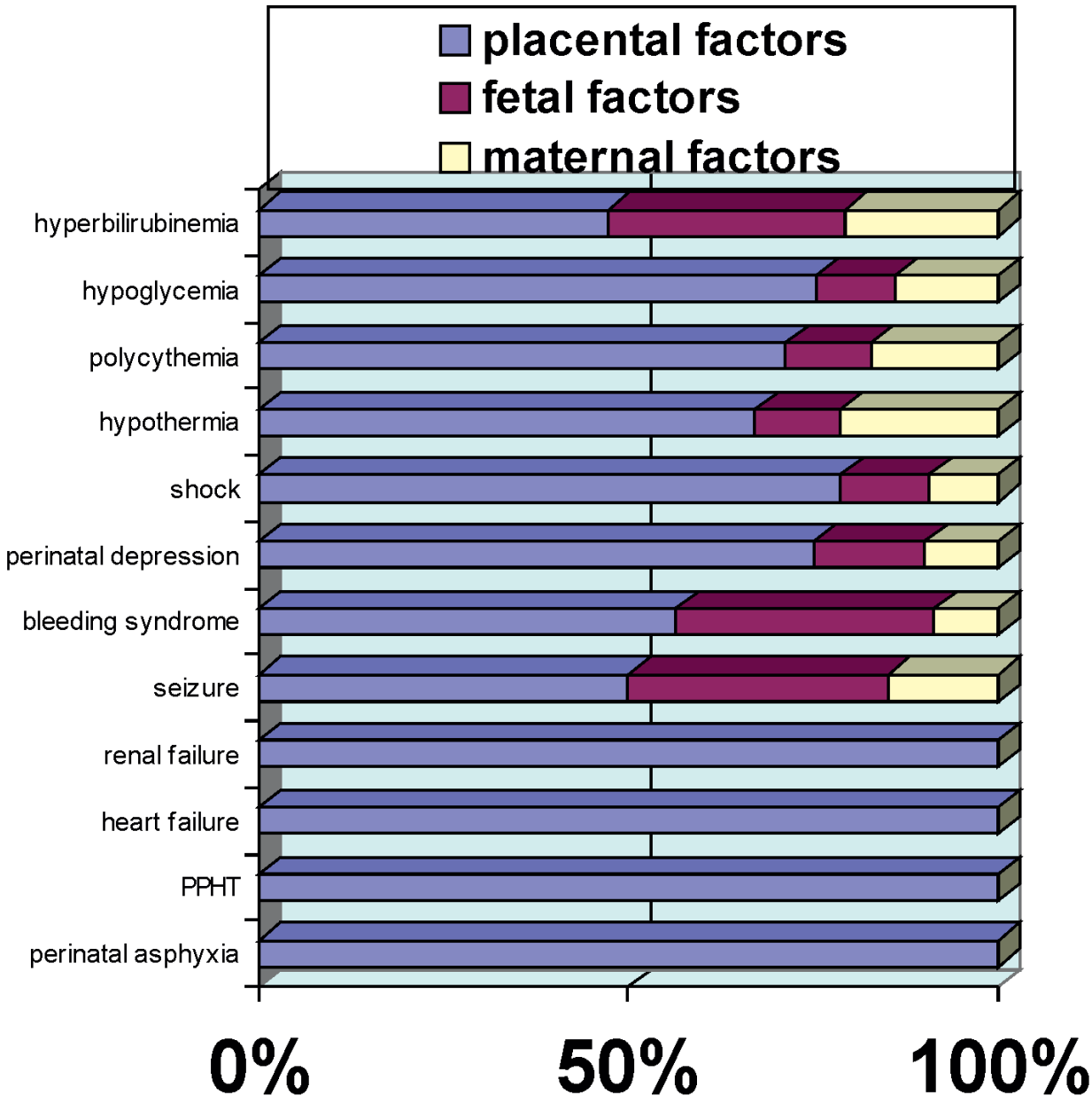

Figure 6. IUGR newborns on term: postnatal complications - comparative representation

Relating neonatal complications to therapeutic management throughout pregnancy we could see that severe pathology (perinatal asphyxia, persistent pulmonary hypertension, post asphyxia heart failure, acute renal failure, neonatal seizures) has appeared in 70 to 100% of the pregnancies not supervised, as follows:

- perinatal asphyxia, persistent pulmonary hypertension, postasphixic heart failure and acute renal failure has appeared only in not supervised pregnancies
- neonatal seizures have appeared in 14 (70%) cases of not supervised pregnancies and in only 6 (30%) cases of supervised pregnancies.

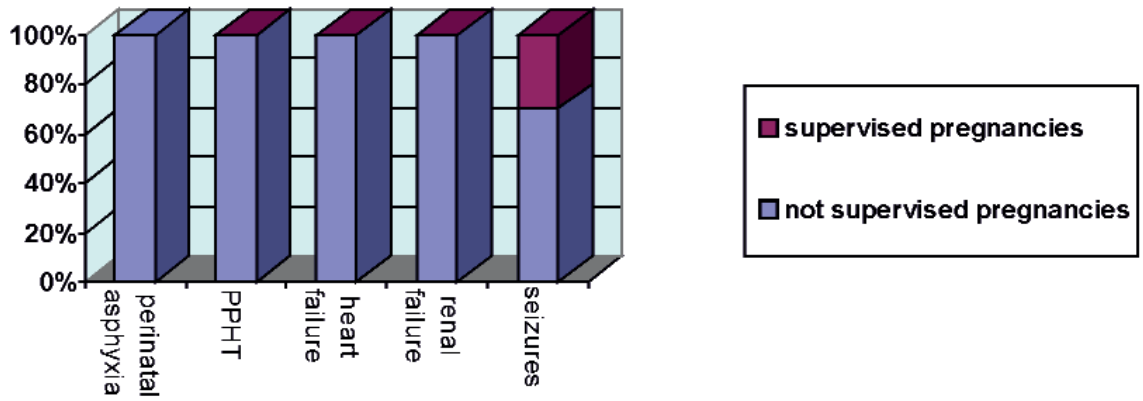

Figure 7. Distribution of major neonatal complications depending on therapeutic management throughout pregnancy

The above data reveal the fact that a small rate (30%) of pregnancies has been observed.

Etiologically, maternal factors have prevailed (low socioeconomic status, constitutional factors, smoking, drug and alcohol use) but the major complications have appeared in cases with placental insufficiency.

Perinatal asphyxia has been avoided in most cases on account of efficient therapeutic management (caesarian sections and adequate neonatal resuscitation). However, in 5 (1,4%) cases this coudn't be avoided ending with death caused by multisystemic asphyxial insult.

SGA preterm newborns

● etiological factors involved:

► fetal factors (multiple gestation, Torch syndrome) – 18 (36%) cases

► maternal factors (low socioeconomic status, extreme age, constitutional factors) – 20 941%) cases

► placental factors (placental insufficiency) – 11 (23%) cases

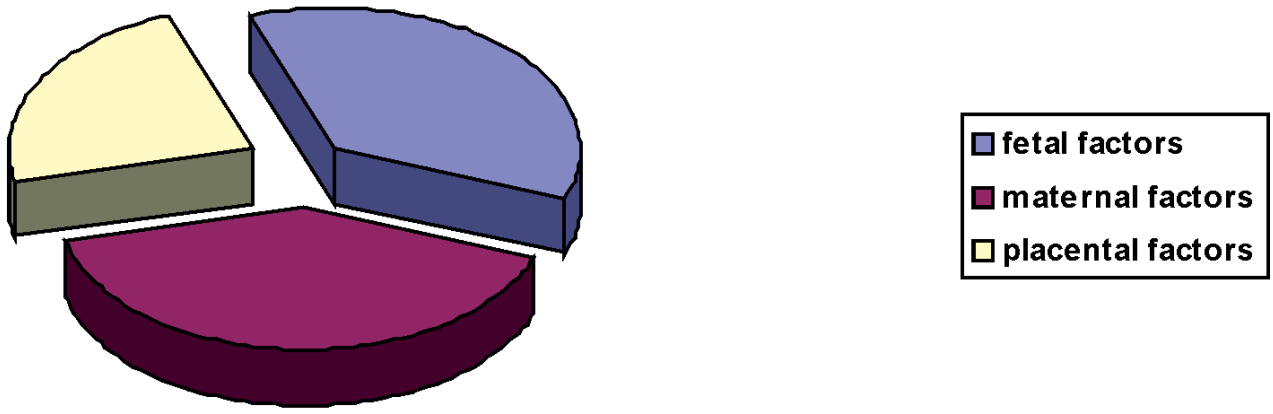

Figure 8. IUGR premature newborns: etiological factors

● according to therapeutic management throughout pregnancy: only 22 (45%) pregnancies have been observed and the same methods mentioned before have been used

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 2, 2012, pp. 225-233

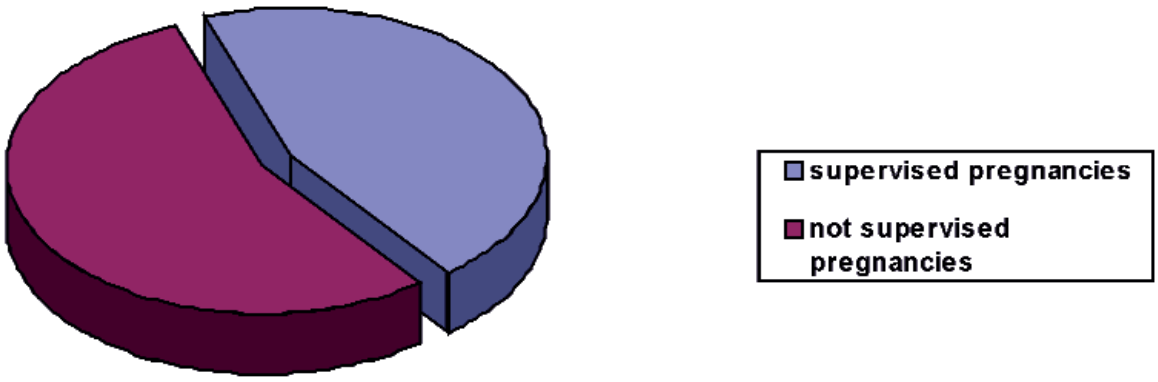

Figure 9. IUGR premature newborns: pregnancy management

● according to birth management: caesarian sections have been performed in 30 (61,2%) cases for fetal distress

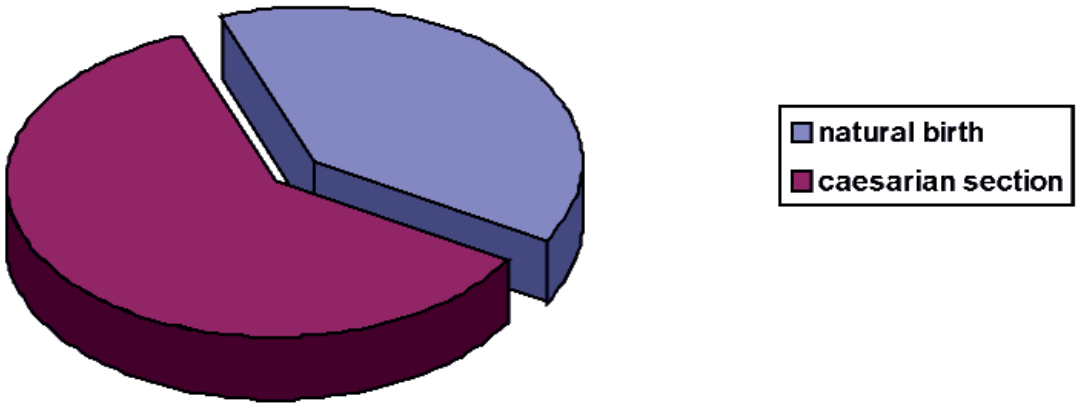

Figure 10. IUGR premature newborn: delivery management

● according to neonatal pathology: moderate perinatal depression – 25 (50%) cases, acute renal failure – 6 (12,2%) cases, neonatal shock – 15 (30,6%) cases, neonatal seizures – 11 (23%) cases, bleeding syndrome (disseminated intravascular coagulation) - 5 (10%) cases, polycythemia – 7 (14,3%) cases, necrotizing enterocolitis – 5 (10%) cases, apnea – 5 (10%) cases, congenital infections – 63 (31%) cases, respiratory distress syndrome – 9 (18,3%) cases, neonatal hyperbilirubinemia – 35 (71,4%) cases

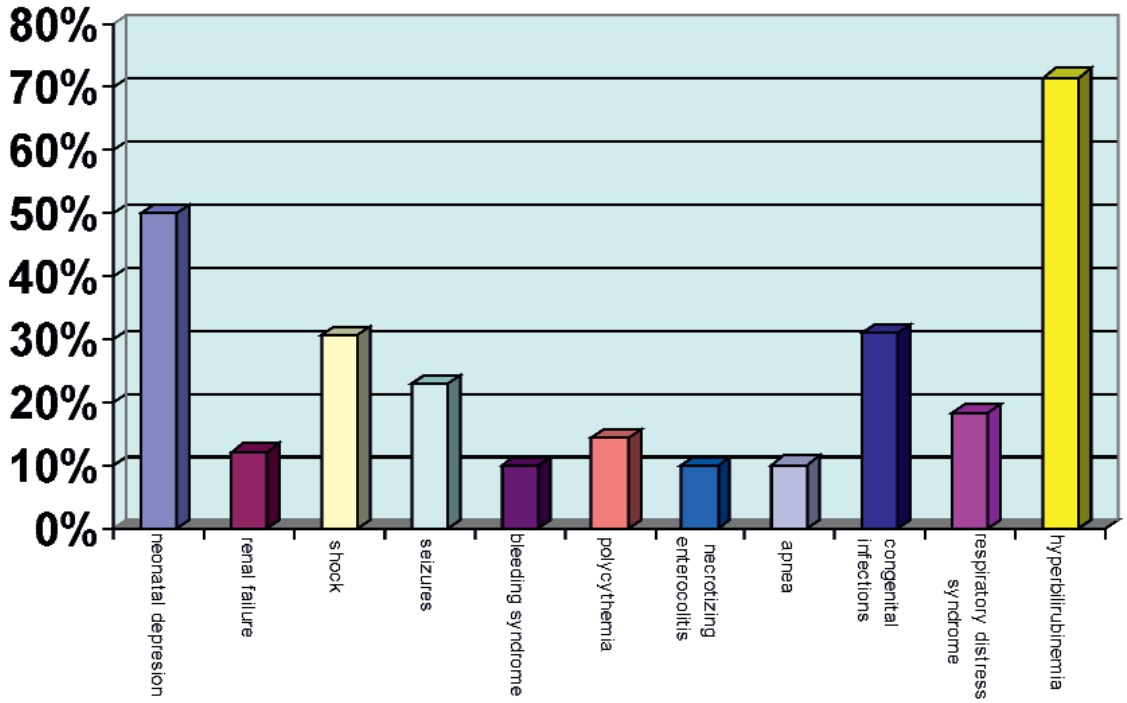

Figure 11. Postnatal complications of premature newborns with IUGR – comparative representation

Comparing the neonatal complications of SGA premature newborns with those of SGA newborns on term, the rate is considerably higher for SGA premature newborns with exceptions of polycythemia.

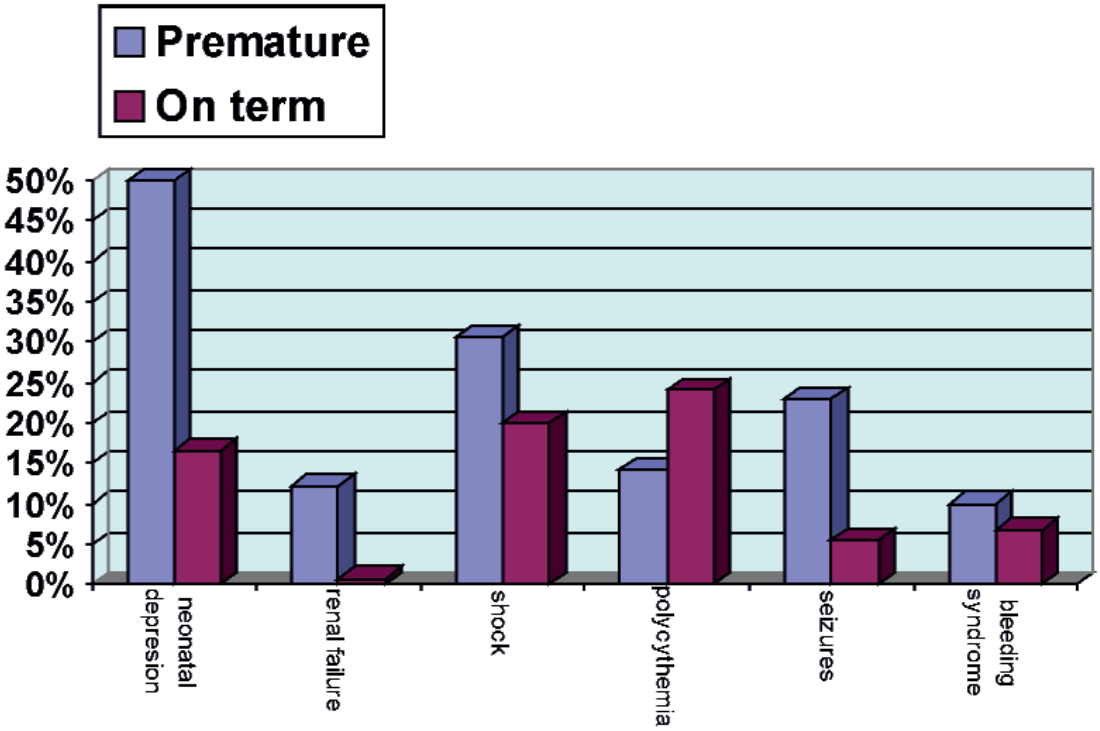

Figure 12. Comparative representation of neonatal complications of SGA premature newborns and of SGA newborns on term

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 2, 2012, pp. 225-233

The data above show that the rate of fetal surveillance in pre-term births is higher than in on term births (45% respectively 33%) with Caesarian sections in 61,2% respectively 17%. Perinatal asphyxia has been avoided through adequate therapy. However, neonatal morbidity was much higher in pre-term SGA newborns as compared to term newborns on account of the existence of prematurity and hypotrophy. 5 (10%) death have been registered because of complications (necrotizing enterocolitis, disseminated intravascular coagulation, perinatal infection) of pre-term newborns. 7 (1,4%) deaths of on term newborns occurred because of perinatal asphyxia.

CONCLUSIONS

► Of all newborns with low birth weight registered in our unit the incidence rate of intrauterine growth restriction and subsequent pathology is much higher than that mentioned in literature (39% respectively 30-33%). Also, the premature births incidence is higher in our unit than in literature data (12%, compared with 6-10%). This is probably mainly due to low socioeconomic status which limits access to adequate surveillance throughout pregnancy and prompt therapy.

► Although etiologically maternal factors have prevailed, the most severe neonatal pathology was mainly due to etiological placental factors.

► Perinatal asphyxia has been avoided by increasing fetal surveillance of pre-term births. However, neonatal morbidity in premature cases was much higher (10% respectively 1.4%) on account of the coexistence of the 2 pathologies (prematurity and hypotrophy)

► Adequate fetal surveillance through Doppler velocimeter and fetal biophysical profile allows efficient intervention (birth decision usually by Caesarian section) and avoids stillbirth or perinatal asphyxia followed by death in neonatal period.

► The collaboration between the obstetrician and the neonatologist as well as the existence of a neonatal resuscitation team and a neonatal intensive care unit allow adequate management of newborns with perinatal asphyxia leading to their prognosis improvement.

► Long-term prognosis in cases with growth restriction depends on the degree of fetal damage and prematurity. The decision of pre-term birth initiation increases the risks connected with prematurity. Unlike the appropriate gestational age premature newborn the SGA premature newborn registers a smaller incidence of cerebral palsy or major neurological damage. However, minor neurological anomalies show a much higher incidence with SGA newborns.

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