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PREMATURE DELIVERY UNDER 32 WEEKS OF GESTATION – CASE CONTROL RETROSPECTIVE STUDY

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Abstract: *Prematurity is a major health problem and it is an important life-threatening pathology for the children in their perinatal, new-born and infantile period. We have evaluated the epidemiologic factors for prematurity in Obstetrics Clinic of Sibiu city. We have analysed the epidemiology of 649 preterm babies between 2012 and 2019 in a III grade Maternity Clinic concerning general maternal information, pregnancy pathology and delivery. We have found significant differences between single and multiple pregnancies and between natural conceived pregnancies and assisted reproductive techniques conceived pregnancies concerning the maternal age, number of cortisone doses, modality of delivery and significant differences between normal conceived and assisted reproductive technique conceived new born related to maternal age and pregnancy and labor fetal presentations dystocia. As a conclusion, prematurity is induced by high blood pressure, pregnancy bleeding and infectious complications. Prophylactic cortisone is improving fetal outcome and is a routine practice in our clinic.*

INTRODUCTION

The incidence of prematurity is dramatically influenced by the quality of prenatal medical network involved in the evaluation, treatment and follow up of the pregnancies.

The incidence of prematurity in Romania is around 10%, sometimes even higher going to 12,5% and it is considered to be much higher than in the western countries of Europe.(1)
The main complications that affect and have a major influence the neonatal prognosis and the long-term prognosis of the premature new born are acute respiratory failure, intraventricular hemorrhages, necrotic enterocolitis, late neonatal sepsis, retinopathy of prematurity, chronic lung disease etc.

The most important factor involved in improving the prognosis of high-grade prematurity is significant investment in the health system. Japan is one of the countries which had a poor prognosis for prematurity and has become one of the most advanced health care system for pregnant and neonatal health care. The main aspects changed for improving the neonatal the prognosis are: maternity birth, the emergence and development of neonatal intensive care services, mechanical ventilation and monitoring of neonatal vital parameters, surfactant therapy, pulse oximetry and high-frequency oscillatory ventilation (HFOV).(2)

AIM

Evaluation of epidemiological factors in premature births under 32 gestational weeks in the Obstetrics and Gynecology Clinic of Sibiu

MATERIALS AND METHODS

All premature babies born in Obstetrics and Gynecology Clinic Sibiu or transferred to our unit (level III) between 2012 and 2019 were included in the study.

Exclusion criteria: readmissions for maternal/ neonatal problems

Neonatal features and postnatal complications among premature infants under 32 weeks were compared; the data were collected from the section's electronic database.

There were collected general information about the pregnancies and information about the determination and favouring factors for premature delivery. Fetal outcome factors were also collected.

Statistical analysis was performed using SPSS for Windows 19.0; p was considered statistically significant <0.05; ORs were calculated for 95% CI

RESULTS

During the period of study, in the Obstetrics and Gynecology Clinic of Sibiu, there were assisted for delivery and were transferred 649 premature new-borns under 32 weeks of gestation. From 583 births the average gestational age of the lot was 29.6 +/- 2.4 (median 30.6), and the average weight was 1347.02 +/- 315.7 (median 1360). According to the weight for the gestational age there were adequate for gestational age 252 (38,8%), small for gestational age 335 (54,6%) and large for gestational age 63 (9,74%).

The distribution of the maternal age is presented in table no. 1.

Table no. 1. Distribution of the maternal age

Maternal age	Number
<18	56
19-34	475
35-39	118
>40	23

The data about number of gestations and parity, an

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important factor in etiology of prematurity the distribution is presented in table no. 2.

Table no. 2. Distribution of gestation and parity numbers

Gestations		Parity	
1	170	1	244
2-4	285	2-4	274
>5	128	>5	65

An important factor which was considered for the etiology of prematurity was the number of the fetuses. The data are presented in table no. 3.

Table no. 3. Number of the fetuses for a pregnancy

Number of fetuses	Number of cases	%
1	484	82,9
2	97	16,6
3	2	0,3

The weight of the new-borns at the delivery is presented in table no. 4.

Table no. 4. The distribution of new born weight at birth

Weight at delivery	Number
<500 g	4
501 – 750 g	40
751 – 1000 g	97
1001 – 1250 g	122
1251 – 1500 g	155
1501 – 1750 g	135
1751 – 2000 g	67
2001 – 2500 g	29

As the number of the fetuses is influenced significantly by the assisted reproductive techniques (ART) such as ovulation induction and vitro fertilization (IVF) the number of pregnancies obtained by ART were evaluated separately. The distribution is figured in table no. 5.

Table no. 5. The modality of obtaining the pregnancy

Type of pregnancy	Number	%
ART	24	3,9
Natural	560	96,1

Premature delivery is also associated with different types of pathology. The most frequent pathology found associated with the prematurity under 32 weeks of gestation were: diabetes 4 (0,7%), 3 with prenatal existence, 1 as gestational diabetes, high blood pressure HTA 45 (7,7%), 7 chronic hypertension, 38 with pregnancy induced hypertension, preeclampsia and eclamsia in 17 cases(2,9%), coriaoamniotitis 6 cases(1%, hemorrhage during pregnancy and labour 54 (9,3%), other pathology in 281 cases (48,2%), 160 cases (27,4%) by imminent premature birth and 35 cases (6%) by urinary infections.

Cortico-therapy is essential in the prevention of fetal respiratory distress. In our study the cortico-therapy was administered and initiated as soon as possible. The situation is this: the average gestational age at the administration of cortico-therapy 30.5 SG +/- 2.4 weeks, prenatal corticosteroid therapy - 334 (57.2%), number of doses:1 dose - 91 (15.6%), 2 doses - 54 (9.3%), 3 doses - 38 (6.5%), 4 doses - 143 (24.5%), 5 doses - 5 (0.9%), 6 doses - 1 (0.2%), 8 doses - 2 (0.3%), complete cure – 151, incomplete treatment – 183.

The average duration of corticosteroid treatment was also determined. The average birth age for the premature new-born was of 30.7 +/- 79 hours. Usually, the corticosteroid used was Dexamethasone in 310 cases and hydrocortisone acetate in 24 cases.

There are important obstetrical factors analysed in our study with important influence in the maternal and new-born prognosis:

Presentation

- Cranial - 490 (75.5%)
- Other (pelvic, transverse) - 159 (24.5%)
- Cesarean delivery - 209 (32.2%)
- With labour triggered - 117 (64.3%)%
- Without - 65 (35.7%)
- Duration of ruptured membranes
- More than 18 hours - 156 (26.8%)
- More than 48 hours - 85 (14.6%)

The pregnancies have different evolution and complications according to the modality of obtaining the pregnancy. The pregnancies obtain by ART procedures are more exposed to obstetrical complications but usually they benefit from a better follow up during the pregnancy. The differences between pregnancies obtained in a natural way or by ART procedures are presented in table no. 6.

Table no. 6. The comparative data between ART and natural pregnancies

	ART	Natural	p
Number	34	618	
Gestation age	29,4+/- 2,5	29,6+/- 2,4	0,652
Weight	1315,7	1349	0,626
Mother age	31,2	28,17	0,008
Gestations	1,8	3,2	0,001
Parity	1,5	2,4	0,003
No. of cortisone doses	3,8	2,7	<0,001
Gender	Male 47,1%	Male 58,5%	0,187
Small for gestational age	38,2%	52,4%	0,638
Diabetes	0	4	0,019
High blood pressure	6	42	0,299
Preeclamsia/eclamsia	0	6	0,546
Bleeding	0	56	0,006
Imminent preterm delivery	22 (64,7%)	152 (24,7%)	0,001
Urinary infections	0	36	0,141
Corioamniotitis	0	6	0,564
Presentation dystocia	35,3%	23,3%	0,133
Cesarean section	64,7%	30,4%	0,001
Spontaneous rupture of membranes more 18 hours	17,6%	25,8%	0,287
Spontaneous rupture of membranes more 18 hours	5,9%	14,3%	0,167
Corticotherapy	82,4%	55,4%	0,002
Full doses corthicotherapty	79%	41,3%	

There are different types of evolution and prognostic, some of them with statistical significance between single pregnancies and twin pregnancies. The data are presented in table no. 7.

Table no. 7. The comparative data between twin and single pregnancies

	Twins	Single	p
Number	165	483	
Gestation age	29,4+/- 2,2	29,5+/- 2,4	0,113
Weight	1359,1	1343	0,646
Mother age	28,8	28,0	0,180
Gestations	2,9+/-2,4	3,2+/-2,6	0,147
Parity	2,6+/-1,9	2,3+/-2,6	0,419
No. of cortisone doses	2,1	2,8+/-1,4	<0,552
Gender	Male 60%	Male 57,1%	0,099
Small for gestational age	46,1%	53,6%	0,242
Diabetes	0	9	0,268
High blood pressure	9	39	0,327
Preeclamsia/eclamsia	3	16	0,620
Bleeding	4	52	0,676
Imminent preterm delivery	42 (26,5%)	131 (27,1%)	0,035
Urinary infections	4	33	0,037
Corioamniotitis	1	5	0,620
Presentation dystocia	37%	20,3%	0,001
Cesarean section	35,2%	31,1%	0,331
Spontaneous rupture of membranes more 18 hours	14%	29,1%	0,001
Spontaneous rupture of membranes more 48 hours	6,1%	16,4%	0,001
Corticotherapy	88%	58,2%	0,279
Full doses corthicotherapty	42,7%	44,8%	0,724
ART	17,6%	1%	0,001

DISCUSSIONS

Analysing the data presented we have found a significant number of premature delivery under 32 weeks of gestation. The average gestational age is about 29 weeks and the average weight is according to the gestational age.

Analysing each case, we have found that a significant proportion of the new-born – 54,6% were small for gestational age. Small for gestational age can be caused, usually by the pathology found as being associated or being the etiology of the prematurity. The most frequent pathology involved in low weight at birth are preeclampsia, chronic hypertension associated with preeclampsia, and the presumption of developing intrauterine growth restriction can be predictive by ultrasound scanning and monitoring. The studies presented in the literature shows a good sensitivity and specificity to ultrasound scan for fetal growth.(3)

Analysing the maternal age, as it was expected the most frequent maternal age is between 19-35 years, the age of maximum fertility, when most pregnancies are registered. There is also a high incidence for infantile pregnancies and for advanced maternal age where medical factors can be involved in the incidence of prematurity. One of the most frequent pathology for infantile pregnancy is premature delivery.(4)

Advanced maternal age is usually associated with chronic disease such as diabetes, chronic hypertension, renal and cardiovascular chronic disease also associated with high grade of prematurity, spontaneous or iatrogenic by obstetrical interventions for vital interest of the fetus or of the mother.(5)

An important factor involved in prematurity is the modality of obtaining a pregnancy. Assisted reproductive techniques are involved in the incidence of prematurity in two major circumstances. One is for single fetus pregnancies obtained by in vitro fertilization (IVF) where the factors are intricated considering advanced maternal age, discussed previously and the other is the perinatal pathology induced by the method itself. IFV pregnancies have higher rate of premature delivery, with new-born admission in intensive care units and congenital malformations. The higher incidence of congenital malformations is usually associated with intracitoplasmatic sperm injection.(6)

IVF pregnancies are also associated with high grade of twin pregnancies which, by itself is responsible for a high rate of premature delivery. In the last twenty years we are assisting to a twin pandemic, and sometimes even higher grades multiple pregnancies. The main reasons are the development of ART and the average advanced maternal age, both factors being responsible for multiple pregnancies. ART is involved by multiple oocytes during ovulation induction, by transferring more than one embryo and by the high fragility of the eggs transferred during IVF procedures. In many cases IVF is associated with advanced maternal age. If ART is causing usually dichorionic twins, single embryo-transfer and advanced maternal age is responsible for monochorionic twins, with a poorer prognosis than dichorionic pregnancies.(7,8,9)

Cortico-therapy is, in our days, unanimously accepted as being a major progress in premature preparation of the new-born, with a better outcome and prognosis. In all the cases, excepting few cases with advanced labour, cortico-therapy was administrated, in the majority of the cases. The initiation of cortico-therapy was present in almost all cases but a complete cure consisting of 4 doses of a cortisone drug was administrated only in 25% of the cases. The average duration of time from cortico-therapy was about 30 hours, usually enough for the prophylaxis of new born respiratory distress. The benefits of cortico-therapy are largely recognized in literature data.(10,11,12)

If we compare and statistically analyse all the factors presented in the results for the modality of obtaining the pregnancy we can see that there are significantly differences between those two categories for the number of cortisone doses and for the incidence of the caesarean section, maternal age, number of gestations, parity, gestational diabetes, bleeding and imminent preterm delivery.

The number of the cortisone dosses is influenced by two factors; – the length of the hospitalization before onset of labour and the prophylactic administration of cortisone before the emergency occurs. Usually, ART pregnancies are considered high risk pregnancies and the follow up is more adequate comparative with natural pregnancies. In ART pregnancies, as in our country transferring two blastocysts is still a routine the twin pregnancies are more often and this is resulting in higher risk of premature delivery.(13,14) Knowing the twin pregnancy is at high risk of prematurity obstetricians are usually administrating cortico-therapy when certain signs are predicting the premature possible birth. The most important signs are shortening and softening of the cervix and higher uterine activity.(15) Recognizing these signs is usually followed by full dose of cortico-therapy and a significant reduction of new born respiratory distress.

Another significant difference is in the modality of delivery for ART pregnancies and for natural conceived pregnancy. For the ART pregnancies the incidence of the caesarean section is more than double.(16) There are a lot of factors to be considered and the first is the higher incidence of multiple pregnancies, especially twin pregnancies with a higher incidence of abnormal presentations such as breech and transvers presentation of one of the fetuses.(17,18) Advanced maternal age is more frequent, the ART pregnancies usually are conceived after a long period of infertility, this long period being associated with progressive advance in the maternal age. Advanced maternal age itself is a high risk pregnancy and the general and different organ pathology associated or induced by the pregnancy are more frequent found in this category of pregnancies.(19)

The other factors analysed between natural conceived and ART pregnancies: gestation range, gestational age, weight, gender, small for gestational age, diabetes, high blood pressure, bleeding, maternal infections, spontaneous rupture of the membranes did not have significantly statistical differences.

Analysing the differences between single and twin pregnancies we could find significantly differences between ART conceived pregnancies, the incidence of the premature rupture of the membranes and fetal or labour dystocia.

Premature rupture of membranes has a double incidence in twin pregnancies, also described in literature data.(20) Twin pregnancies are much often associated with cervical softening and ripening, much earlier than in single pregnancies. Cervical dilatation is more often seen in twin pregnancies due to rapid increase in uterus size and premature formation of the lower segment of the uterus. Associations of local infections such as Streptococcus B or Ureaplasma infections are inducing a local inflammatory response with degradation of the patency of the membranes and premature rupture.(21,22)

Labour dystocia and abnormal presentations such as breech, transverse or oblique position of the fetuses are more frequent associated with twin pregnancy and this type of pathology is a common indication of caesarean section.(23)

All the other parameters considered for a comparison between single and twin pregnancies did not have statistical significance.

CONCLUSIONS

1. Prematurity is a public health problem due to the large

number of new-borns, especially those with gestational age under 32 weeks of gestation.
2. The main causes of prematurity under 32 weeks were HTAIS, pregnancy bleeding and infectious complications.
3. Prophylactic cortisone therapy is improving fetal outcome by preventing new born respiratory distress and is a routine practice in our clinic.
4. In the comparative analysis between multiple and single pregnancy there are significant differences in maternal age, in terms of premature rupture of membranes and fetal dystocia, and ART conceived pregnancies.
5. In the comparative analyses between natural conceived pregnancies and ART pregnancies we have found statistically significant differences the number of cortisone doses and for the incidence of the caesarean section, maternal age, number of gestations, parity, gestational diabetes, bleeding and imminent preterm delivery.

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