

## PERINATAL ASPECTS IN NEWBORN RESULTING FROM ASSISTED HUMAN REPRODUCTION

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### Abstract

The paper present the main aspects of perinatale evolution of new – born resulting from assisted human reproduction compared with those resulting from natural reproduction in Vitro Fertilization Center within the Obstetrics – Gynecology Clinic „Bega” Timișoara. The study validates The results obtains during 10 years of experience in the team of the country first in Vitro Fertilization Center.

The researched material is represented by a group of 109 new – born resulting from assisted human reproduction who were delivered in the clinic. These cases were completely monitored until going home. A control group (n = 95) represented by new – born resulted from natural reproduction was used for the factorial analysis and the accuracy of the results. The method of controlled comparative research was used (case - with ness). The main perinatal risk factors as well as the evolution parameters of the new – born during the first week of life have been analyzes.

There are no significant differences for most of the analyzed parameters between the cases of the two groups. Important differences were registered for: the average age of the mother (higher in the researched group); the monitorization of the gestation evolution (better in the research group); delivery through caesarian section (more frequent in the research group); the incidence of prematurity and intrauterine growth limitation and their perinatal/neonatal consequence (higher and more important in the research group); the incidence of multiples pregnancies (exclusively in the research group). The results are validated by the size of the groups and the analyzed method.

The results of the study show that the perinatal evolution of the new – born is mostly independent of the way of conception and it depends on the fetu – neonatal status of the perinatal period. Assisted human reproduction represents a great victory of medicine against sterility.

**Key words:** newborns, human assisted reproduction.

### Introduction. Objectives

Ten years ago, in the “Bega” University Clinic for Obstetrics and Gynecology of Timișoara, the bases were laid for the first Human Assisted Reproduction (HAR) Centre in Romania. Its creation was one of the recent achievements of medicine, if we take into account the fact that the first baby resulted from in Vitro Fertilization and Embryo – Transfer (FIV/ET) was born in England in 1978

(Edwards et al). Since then, thousands of babies are born every year as a result of this technique. The HAR Centre in Timișoara has had results similar to those of the largest centers in the world.

In the center data base there is a significant number of parameters, such as: causes of infertility (which led to the HAR’s decision), specific investigation means to determine the women or couples which can benefit from this technique, fertility rate, pregnancy rate, etc. These date do not form the subject of the present study, but they can be included globally as guide mark.

Globally analyzed, the obstetrical pathology of the mother who turned to the HAR is significantly more charged with spontaneous or provoked miscarriages, as well as with one or two ectopic pregnancies. These accidents appear with a frequency of about 50%, explaining the primary or secondary tube sterility. The pathologic events of these cases interest more the reproduction organs and in a lower measure the other systems and organs (especially the endocrine system) with impact upon the reproduction function.

For a long time the woman’s sterility was believed to guide a couple towards the HAR. Nowadays it is admitted that the masculine sterility is a very frequent reality which can determine a couple to make a FIV/ET.

All the mentioned data are important to obtain a pregnancy, after one or more previous experienced resulting in reproductive failure. They interest particularly the following fields: embryology-genetics, gynecologic endocrinology and obstetrics gynecology; these specialists realize the team of a HAR center and are permanently preoccupied by the optimization of the technologies leading to an ever higher pregnancy rate (the percentage ratio of the number of pregnancies obtained and the number of FIV/ET realized).

Concerning the perinatal period, the birthrate for HAR babies seems very important. For neonatology the “take home baby” rate is very important, that is the number of newborns integrated in their families as to the total number of births resulting from HAR, compared to the newborns resulting from natural reproduction (RN).

The HAR methods offer to a couple labeled as “sterile” the chance to have a baby. Once the pregnancy installed, its evolution does not differ from a Natural Reproduction (NR) pregnancy, being exposed to the same risks. The significant difference is the higher number of multiple pregnancies (double or triple) in HAR, as a consequence to the present FIV/ET techniques.

Thus, in order to increase the pregnancy chances to obtain a unique pregnancy, ET is performed with a number of 3 – 6 embryos. In such conditions the probability to obtain a twin (double or triple) pregnancy increases. The continuous improvement of the HAR techniques allows the performance of ET with a single embryo, but reduces the chances of pregnancy.

Coming back to the results of the HAR Centre in Timișoara, up to now the “take home babies” rate has been over 500 babies, adding up all the centers in Romania where babies resulted from HAR were born. Out of these, only 109 were born in the “Bega” University Clinic.

The objective of the research is the analysis of physical and functional parameters as well as of adaptation issues and precocious neonatal pathology in the group of

newborns resulting from HAR, compared to a control group representing newborns resulted from NR which followed a HAR birth. Together with the above mentioned parameters, certain essential perinatal data were selected as comparison landmarks between the two groups.

**Material And Method**

The studying material is represented by a group of 109 HAR resulted newborns at the FIV/ET Center of the “Bega” Clinic and a comparable group of 95 NR resulted newborns at the same center selected following the case-control study pattern, that is after the birth of a HAR baby and included in the study group, the following newborn resulting from NR was included in the control group (table I).

Table I. The study lot. Cases distribution using year’s study

<b>Year’s study</b>	<b>Nr. of the birth</b>	<b>Nr. de newborns</b>	<b>Twins Double</b>	<b>Twins Triple</b>
1995-1996	4	4	-	-
1996-1997	7	7	-	-
1997-1998	8	8	-	-
1998-1999	10	10	-	-
1999-2000	11	11	-	-
2000-2001	10	13	1	1
2001-2002	10	10	-	-
2002-2003	10	13	1	1
2003 - 2004	13	17	4	-
2004 -2005	12	16	2	1
<b>Total</b>	<b>95</b>	<b>109</b>	<b>8</b>	<b>3</b>

The difference in numbers between the groups results from the fact that in the study group there were five twin pregnancies (two double and three triple), whereas in the control group there were only single pregnancies. In all the cases included in the study the significant parameters for comparison according to the study pattern were followed:

- mother’s age;
- pregestation ± gestation maternal pathology;
- gesta – para categories;
- birth modality (± birth incidents);
- gestation age (newborn category);
- anthropometric indices (newborn category);
- special newborn categories (“high” prematurity, twin);
- immediate neonatal adaptation (APGAR score);
- neonatal adaptation issues: initial weight loss, neonatal jaundice, metabolic adaptation, etc.;
- feeding initiation and continuation;
- share of breastfeeding during the first 72 hours;
- release from hospital and integration in the family; average hospitalization;
- cost – efficiency ratio;

- medical follow-up, evolution, prognostic;
- subsequent social insertion.

These parameters were considered important for the comparative analysis and, they were illustrated and discussed.

At the primary analysis of the cases we did not register important differences concerning the sex, area or source distribution. As to the social-economical and cultural level, it is clearly favorable to the study group, since HAR represents an expensive medical procedure, and the insurance system in our country does not cover for it. We did not register significant differences between the groups regarding the gestation pathology either; as to the preexisting parental pathology, the significant difference in the study group is given by the pathology of the genital system which led the couple to choosing FIV/ET.

**Results and Discussions**

Significant differences between the two groups were registered referring to the mother’s age (Table II). Almost half of the mothers in the study group range in the risk group (36 – 40 years old) or even of very high risk (over 40 years of age). By comparison, in the control group there is a “normal” distribution of the mother’s age, similar to the general population for the NR.

Table II. Cases distribution using mother's age

Age (years)	≤ 20	21-30	31-35	36-40	> 40	Total
Study lot	-	23	39	23	10	95
Control lot	8	57	20	9	1	95

Generally, the couples who turn to HAR do it after failing several times in biological reproduction trials, finally accepting (sometimes at a "risk" age) the HAR techniques as a last chance of having a child.

The mentioned aspect is largely found in the distribution of the cases according to the obstetrical past of the mother (Table III).

Table III. Cases distribution using the obstetrical mother's past

Gesta/Para	GIPI	GIPII	GIPIII	G>IIPI	GIPII	GIPIII	GIPIII	G>IIIP>III	Total
Study lot	49	7	9	24	6	-	-	-	95
Control lot	16	15	7	4	27	4	8	14	95

The study group is significantly dominated by primiparous women and multiparous women. By comparison, in the control group there is a balanced distribution of the gesta/para category.

In the primiparous category in the study group are included the women at the first gestation experience irrespective of the biological age and who, besides HAR, presented a previous reproductive failure. This category is significantly dominant (over 50%) and represents an argument concerning the correct indication for the HAR.

The other cases of the study group (the multiparous/primiparous category) experienced partial failures in reproduction since previous pregnancies concluded in abortions, which motivated them to accept the HAR techniques (after a severe "inventory" of the causes leading to reproductive failure).

Due to its high cost, a pregnancy resulting from HAR is more severely followed and monitored, and the pregnant women attend rigorous prenatal checking.

By comparison, in the control group, only primiparous or secundiparous mothers seem more motivated to attend rigorous follow-up of the pregnancy.

Prenatal checking, periodical investigations, early detection of certain diseases during the pregnancy and their treatment of prophylaxis are more rarely or infrequently recorded in the cases of the control group (mostly in the multiparous category). Nevertheless, we have not registered significant differences between the two groups concerning the primary gestation or pregnancy induced pathology.

We have also registered eleven twin pregnancies in the study group (eight double and three triple), which represents 11,57%, by comparison, in the control group we have not registered any twin pregnancy.

The way of giving birth represents a significant difference compared to the control group.

The high risk as well as the higher frequency of risk age in the mother and the need of an increased protection of the fetus, leads to the significant increase of the cesarean operation births in the study group. The high frequency of prematurity, twin pregnancies and low weight at birth in the HAR cases are also adding up.

The distribution of the cases according to the gestation age and birth weight (fig. 1 and 2) shows clearly this difference.

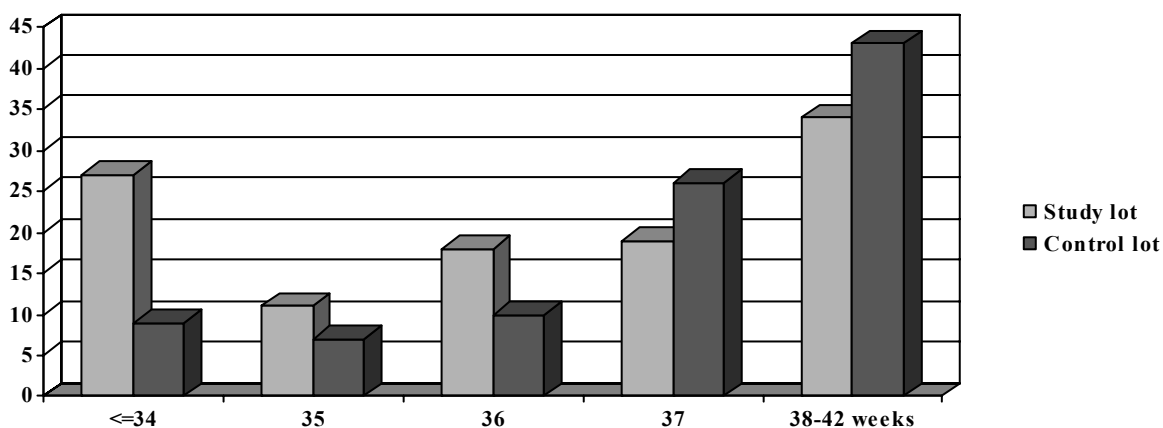


Fig. 1: Cases distribution using gestational age (weeks).

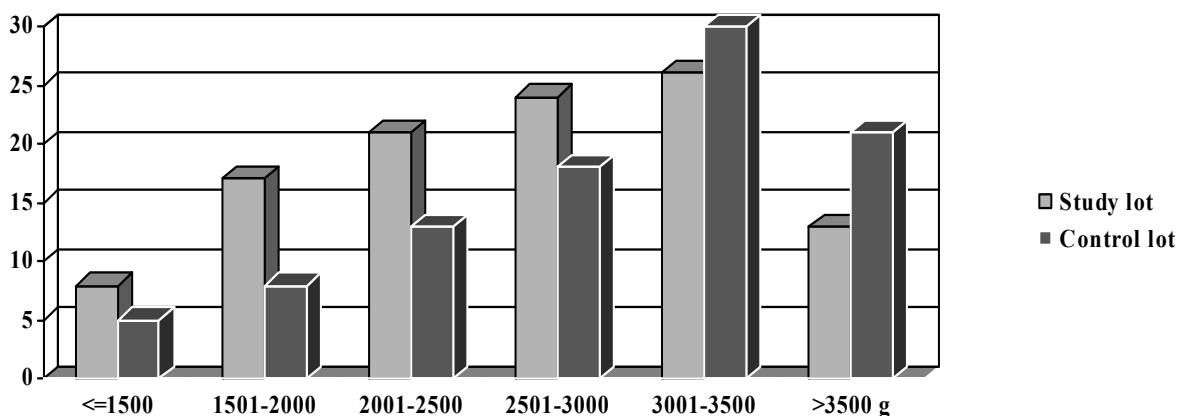


Fig. 2. Cases distribution using birth weight (g).

Thus, in the study group, a significant percentage of newborn have a gestation age  $\leq 36$  weeks and a birth weight  $\leq 2500$ g.

By comparison, in the control group, the frequency of these categories is significantly lower.

The issues mentioned for the study group are also reflected in the immediate neonatal adaptation, shown by the APGAR score at birth (fig. 3).

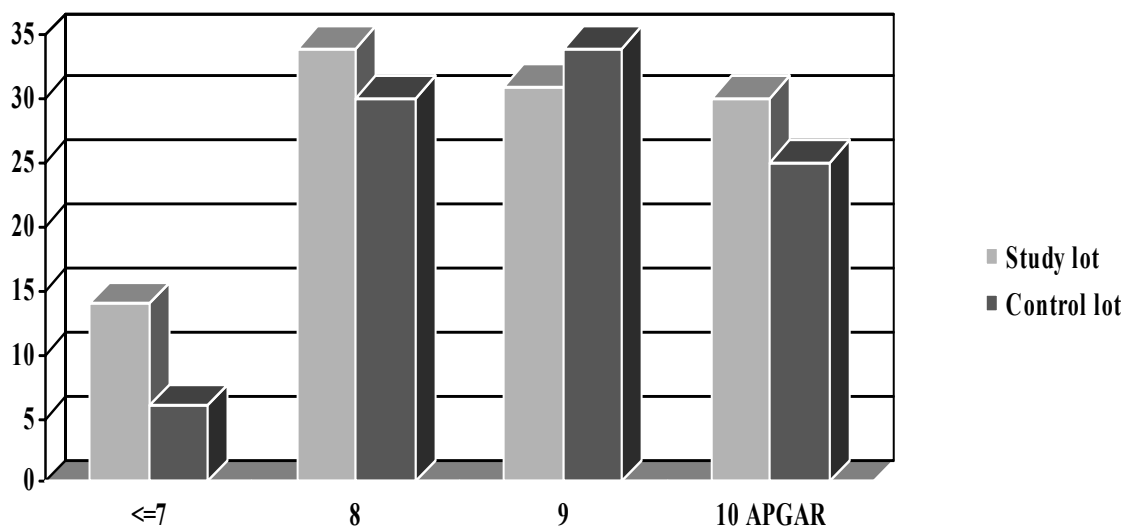


Fig. 3. Cases distribution using APGAR score at birth.

Irrespective of all the precaution measures and the higher anticipation degree of birth problems, the APGAR quotation is much better in the cases of the control group. This fact is greatly due to the higher frequency of caesarian births in the cases of the study group; in most situations it comes to an iterative caesarian, without labour and without immediate adaptation reaction caused by the “catecholaminic wave” which accompanies the natural birth. In such conditions, the adaptation of the newborn

extracted by caesarian is often more difficult due to the slower resorption of the bronchial-pulmonary liquid. But in a global analysis there are no important differences between the two groups, both in immediate adaptation and during the first days of life.

In the figures 4 and 5 we quantified and compared two major problems of the precocious neonatal period, the initial weight loss (% as to the birth weight) and the duration of the neonatal jaundice (days) respectively.

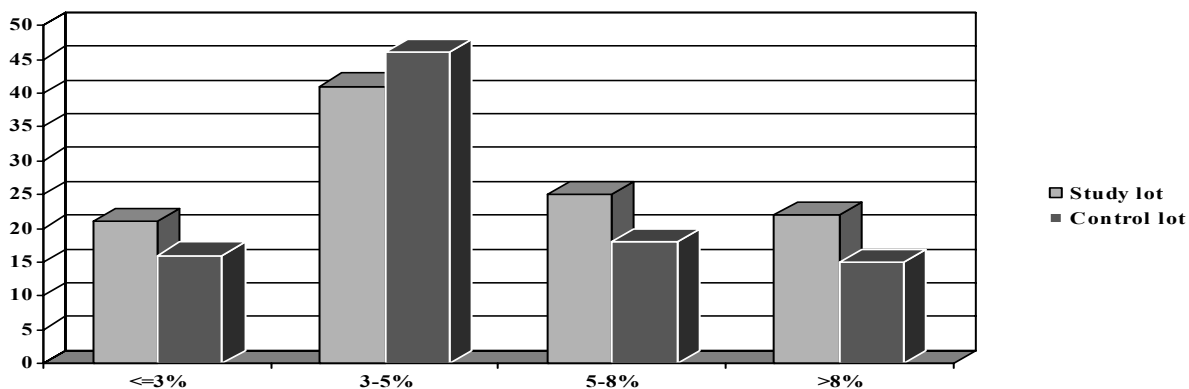


Fig. 4. Cases distribution using the initial weight diminution (% against the birth weight).

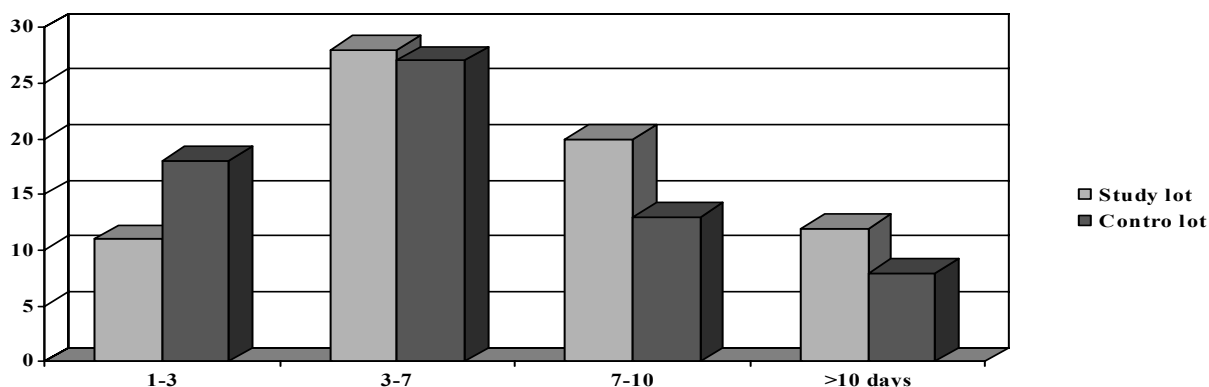


Fig. 5. Cases distribution using the jaundice's length (days).

Top be noticed that both the intensity (proportion) of the initial weight loss and the duration of the jaundice are significantly higher in the cases of the study group. This can be largely explained by the higher frequency of prematurity and twin pregnancies in the HAR cases by comparison to the NR cases.

An important parameter followed in the study was the initiation of feeding in the neonatal period and the share of the natural feeding. Therefore, in our clinic the modern

concept of early initiation of natural feeding in healthy newborns (during the first 3 – 6 hours of life) and of the early enteric feeding in any category of newborns (including small premature babies), irrespective of the kind of feeding, but using human milk as much as possible has the precedence.

We have analyzed comparatively the age of initiation and the share of breast feeding during the first 72 hours of life in the two groups (fig. 6).

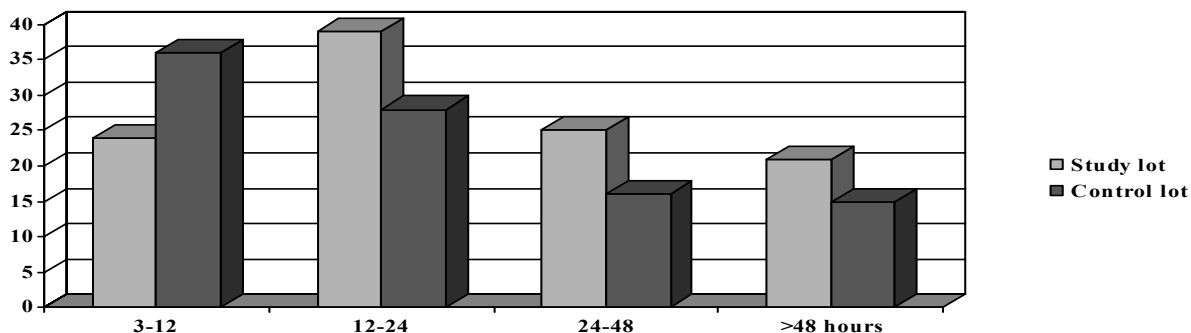


Fig. 6. Cases distribution using the age of nourishment originating (hours).

We have found in both parameters a sensible and significant superiority of the cases resulting from NR and a higher flexibility in initiating and continuing postnatal feeding. The explanation is found in the higher frequency

of prematurity (later initiation of feeding) and higher frequency of caesarian births (later initiation of lactation) in the cases derived from HAR as compared to those derived from NR.

By continuing the research of the parameters taken into account, we registered a significant difference concerning the average hospitalization period and the duration of medical care given in the neonatology department. This parameter represented 10.7 days for the HAR resulting newborns compared to 5.6 days for the NR resulting newborns. According to this result the cost of postnatal care are much higher in the first category.

As to the morbidity during the neonatal period, there were no differences registered between the two groups, all the cases being integrated in their families after the initial recovery. No death was registered in the cases studied and followed up.

Their evolution was good and they all range between the optimal parameters of neuron-psychomotor and physical development according to the biological age. The medical follow-up showed a more frequent and stronger psycho-affective and especially social protection in the newborns and children resulting from HAR, who benefit from better social and economical conditions as compared to those resulting from NR.

#### Conclusions

1. RUA represents a real victory for medicine against sterility. Because of its results, HAR Center of University "Bega" Clinic from Timișoara, is registered in the circle of the greatest profile around the world.

2. The evidence, the pursuit and the monitorization of pregnancies and births which became from HAR, with a better anticipation and preventing maternofetal pathology problems, occur now advantageously and having better results comparatively with the previous pregnancies and natural births.

3. The high risk degree, and also the important prematurity and twins frequency explain the high frequency of caesarian birth at HAR cases; we add here the mother's age risk, significantly increased at the study lot.

4. There is an prematurity proportion, fetus hipotrophy and twins to the cases which became from HAR. Starting from this reality, there are some important differences between the two lots, as you can see:

→ the newborns became from HAR present an important frequency of neonatal adaptation and they need special nursing in the intensive therapy unit ;

→ initial decrease balance is bigger, and the initiating of nourishment is being realized later at the newborns which became from HAR; in the same time, the breast nourishment balance in the first 72 hours is significant low at this category vis a vis of newborns resulted from NR;

→ there are not significant differences about the intensity and the duration of newborn icterus at the two lots;

→ important differences appear concerning the average hospitalization duration period: 10,7 days for the newborns resulted from HAR instead of 5,6 days at the newborns resulted from NR; in key with this postnatal nursing costs are higher than the first category.

5. The study results underline that after birth, the biological child's evolution is mostly independent of the modality of conception and more dependent of the neonatal fetus status in the perinatal period. So psycho-affective and social protection seems to be more important for the newborns resulted from HAR.

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