

The Outcome of Multifetal Pregnancy Reduction in a Perinatal Unit For The Period 1994-2002

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ABSTRACT

THE OUTCOME OF MULTIFETAL PREGNANCY REDUCTION IN A PERINATAL UNIT FOR THE PERIOD 1994-2002

Aims: This study was undertaken to evaluate the pregnancy outcome in women who underwent multifetal pregnancy reduction at a single institution.

Methods: The data reported here reflect the multifetal pregnancy reduction experience of Hacettepe University Hospital Department of Obstetrics and Gynecology, Division of Perinatology from 1994 through 2002. Pregnancy records were retrospectively reviewed.

In the absence of any abnormal findings, the fetuses most readily accessible were chosen for reduction, usually those most fundal in location. All multifetal pregnancy reduction procedures were performed between 9 and 14 weeks gestation via intrathoracic injection of potassium chloride under ultrasonographic guidance.

The fetus chosen for reduction was the one with suspicious ultrasonographic findings such as increased nuchal translucency thickness or delayed growth in comparison with others.

Results: 100 procedures were performed on 93 pregnancies. Of these pregnancies 64 (71,91%) were triplets, 18 (20,22%) were quadruplets, 6 (6,74%) were quintuplets and 1 (1,12%) was a sextuplet.

Mean age of patients was 30,86±4,24, mean gestational age at MFPR was 10,8±1,03, mean starting number was 3,4±0,8 (3-6) and finishing number was 2.

Fetal loss rates according to starting number of fetues were 6,25% for triplets, 16,66 % for quadruplets, and 28,57% for quintuplets and sextuplets. Total fetal loss rate was 10,11%.

Keywords: Multifetal pregnancy reduction, embryo reduction, fetal loss, immature labour

During the last 20 years, there has been a dramatic increase in multiple births. In a population-based study in Denmark, from 1980 to 1994, it was observed that the twinning rate increased 2,7-fold and the triplet-rate increased 9,1-fold. More interestingly, the proportion of multiple births among infant deaths increased from 11,5 to 26,9% during this period [18]. In a US study from 1980 to 1997, twin births have doubled and triplet and higher order pregnancies have quadrupled [16]

This increase in multiple gestations is partly due to assisted reproductive technologies and ovu-

lation induction agents and partly due to increased age of reproduction in women.

Multiple gestations are associated with an increased frequency of maternal complications and higher perinatal morbidity and mortality [12,15]. The major maternal complications are preeclampsia, postpartum hemorrhage, hydramnios and increased cesarian sections. The neonatal complications are due to prematurity or fetal growth restriction. In a review of 12 publications, it was analyzed that of 707 triplet pregnancies 90% of which were delivered before 28 weeks, the perinatal mortality rate was 119 per thousand. These children had increased incidences of developmental disability and cerebral palsy [3]. There is an obvious socioeconomic strain on the family with high order gestations.

Complications increase as the number of fetuses increase. In the FIVNAT study stillbirth rate (30,2 versus 13,5) and early neonatal mortality rate (26,7 versus 18,9) were significantly higher in triplets compared to twins [11].

It is well accepted that multifetal pregnancies are best avoided by the use of strict criteria for ovulation induction and and embryo transfer in in vitro fertilization (IVF). However, when such pregnancies occur despite adequate precautions, multifetal pregnancy reduction may improve the outcome of these pregnancies.

Multifetal pregnancy reduction was initially used as a procedure to selectively terminate a fetus affected by a genetic disorder [1]. Later its usage was extended to eliminate one or more fetuses of a multiple gestation pregnancy [4].

There are certain complications associated with MFPR and the ethical issues are still unclear. This study was designed to evaluate the pregnancy outcome in women who underwent multifetal pregnancy reduction from 1995 through 2002 at our center.

MATERIAL AND METHODS

This study is a retrospective review of the outcomes of 93 pregnancies who underwent 100 multifetal pregnancy reduction procedures at Hacettepe University, Department of Obstetrics and Gynecology, Unit of Perinatology from January 1994 to, January 2002. Selective terminations were excluded from the study.

Multifetal pregnancies were referred to the Unit of Perinatology at Hacettepe University, Department of Obstetrics and Gynecology. All of them gave informed consent about the procedure. Pregnancy records were retrospectively reviewed.

In the absence of any abnormal findings, the fetuses most readily accessible were chosen for reduction, usually those most fundal in location. All multifetal pregnancy reduction procedures were performed between 9 and 14 weeks gestation via intrathoracic injection of potassium chloride under ultrasonographic guidance transabdominally.

The fetus chosen for reduction was the one with suspicious ultrasonographic findings such as increased nuchal translucency thickness or delayed growth in comparison with others.

After the procedures, all of the pregnancies were called for a follow-up visit at 1 week and later at monthly intervals.

RESULTS

100 procedures were performed on 93 pregnancies. Of these pregnancies 64 (71,91%) were triplets, 18 (20,22%) were quadruplets, 6 (6,74%) were quintuplets and 1 (1,12%) was a sextuplet.

Mean age of patients was $30,86 \pm 4,24$, mean gestational age at MFPR was $10,8 \pm 1,03$, mean starting number was $3,4 \pm 0,8$ (3-6) and finishing number was 2.

Fetal loss rates according to starting number of fetuses are summarised in Table I. It can be clearly seen that the fetal loss rate increases as the starting number of fetuses increases.

Around 20% of the deliveries occurred prior to 34 weeks after MFPR, almost half of which were fetal losses (Table 2).

Pregnancy complications observed in the study group are summarised in Table 3.

Table 1. Fetal Loss Rates According to Starting Number of Fetuses

	Loss<20 weeks	Loss btw 20-28 weeks	Total loss
3→2 (64)	1 (1,56%)	3 (4,68%)	3 (6,25%)
4→2 (18)	2 (11,11%)	1 (5,55%)	3 (16,66%)
5→2 ve 6→2 (7)	2 (28,57%)	-	2 (28,57%)
Total loss	5 (5,61%)	4 (4,49%)	9 (10,11%)

Table 2. Gestational Age at Delivery After MFPR

	number	%
Abortion	5	5,61
Delivery btw 20-24 weeks	4	4,49
Delivery between 28-34weeks	10	11,23
Delivery> 34 weeks	70	78,65

DISCUSSION

Table 3. Pregnancy Complications After MFPR

	number	%
Preterm Birth	53	59,55
Preterm rupture of membranes	10	11,23
PIH	8	8,98
Preeclampsia	4	4,49
IUGR	10	11,23
Stillbirth	0	-
Early neonatal death	4	4,49

The total fetal loss rate calculated in this study is similar with certain other multicenter series reported. Fetal loss rate of 337 reduced pregnancies from 1985 to 1992 was 11,86% [5] and of 1453 pregnancies from 1993 to 1996 was 12,3% [10]. Bollen et al compared fetal loss rates after 3 different methods of embryo reduction by several authors and calculated 19,6% loss rate after transcervical aspiration, 12,6% after transabdominal and 9,8% after vaginal approach [6]. The results of a multicenter study from 5 countries revealed that out of 3513 MFPR procedures, the fetal loss rates prior to 24 weeks were 4,5% in triplets, 7,3% in quadruplets, 11,5% in quintuplets and 15,4% in sextuplet and higher order pregnancies. [9] In our study since the number of quintuplets and sextuplets are too small, the fetal loss rate was found to be 28,5% in this group, which must be further investigated with higher number of cases.

In our series, preterm birth was observed in 59,55% of the cases and PROM was observed in 11,23%. In a review of the world results of MFPR from 1993 to 1996, preterm birth rate was 47,7% [10]. Prematurity in multiple pregnancies is a problem in terms of both morbidity and long term sequelae and for the high costs associated with long needs of neonatal intensive care.

Callahan et al reported that 78% of the high-order (≥ 3) multiple pregnancy fetuses were admitted to the neonatal intensive care unit (NICU) and the predicted total charges to the family for triplets was 36.558 US Dollars per baby compared to 18.974 US Dollars per baby for twins [7]. Yaron et al found that the reduction of triplets to twins significantly reduces the risk for prematurity and low birth weight and may also be associated with a reduction in overall pregnancy loss [17]. In this study it was revealed that non-reduced triplets have 25% fetal loss rate, compared to triplets reduced to twins with a 6,2 % loss rate and unreduced twins with 5,8- 6,3% loss rate. Haning et al analyzed 274 IVF pregnancies and calculated that at the 8-week ultrasound, each viable fetus could be expected to reduce the duration of gestation by approximately 3,6 weeks and each fetus reduced medically or spontaneously could be expected to prolong the gestation by 3 weeks [13]. Unfortunately only 13-14 % of triplets undergo spontaneous reduction [13,14]. In contrast to the above studies Leondires et al reported that the perinatal mortality, gestational age at delivery and take-home infant rate per delivery were not changed significantly after reduction of 46 triplets to twins when compared to 81 triplets managed expectantly. (13% of which

were reduced spontaneously) [14]. Alexander et al compared the obstetric outcomes of 32 twin pregnancies obtained as a result of pregnancy reduction with 42 in which reduction had not been used and found that impaired fetal growth and prematurity were not reversed completely by this procedure [2]. Since there are some studies reporting worse and some other studies reporting better outcome with reduced triplets, the ongoing debate about whether triplet pregnancies should be reduced or not, should be answered by every institution's own neonatology unit statistics.

It seems that there is still a high overall fetal loss rate and prematurity after embryo reduction procedures. The most reasonable approach seems to be a consensus to avoid multiple pregnancies in ART programmes. However there are certain obstacles for such a solution.

The teams in IVF are not always the same as the obstetrical ones who follow up the pregnancies and their obstetrical complications. As a result certain facts are not very well known to these teams. An example is the fact that a twin pregnancy, even though less complicated than triplets induces 42 % of prematurity (of which 55% are less than 32 weeks) and 3% of perinatal mortality [8]. Another fact is that the couples themselves are unaware of the difficulties of multiple pregnancies so that there is a pressure on IVF teams to replace maximum number of embryos. One of the most important shortcoming is that not all teams have a good cryopreservation programme so that they try to replace as many embryos as possible to give their patients maximum chances to get pregnant. However it must always be kept in mind that the real success of an IVF team is not the pregnancy rate but the take-home baby rate and even further the rate of healthy babies with a good developmental outcome in future. For this reason, the prevention of multiple gestations must be the goal of future studies rather than reducing the number once pregnancy is achieved. Every effort must be put in to issue guidelines for the prevention of higher order gestations by multidisciplinary commissions formed by Neonatologists, Perinatologists, Reproductive Endocrinologists and Psychologists.

REFERENCES

1. Aberg A, Mitelman F, Gantz M et al. Cardiac puncture of fetus with Hurler's disease avoiding abortion of unaffected co-twin. *Lancet* 1978; 2: 990-991.
2. Alexander J, Hammond K, Steinkampf M. Multifetal reduction of high order multiple pregnancy : comparison of obstetrical outcome with non-reduced twin gestations. *Fertil Steril* 1995; 4: 1201-1204.

3. Berkowitz RL, Lynch L, Alvarez M. The current status of multifetal pregnancy reduction. *Am J Obstet Gynecol* 1996; 174: 1265-1272.
4. Berkowitz RL, Lynch L, Chitkara U. et al. Selective reduction pregnancies in the first trimester. *N Engl J Med* 1988 ; 318: 1043-1047.
5. Benschushan A, Lewin A, Schenker JG. Multifetal pregnancy reduction: Is it always justified? *Fetal Diagn Ther.* 1993 ; 8: 214- 220.
6. Bollen N, Camus M, Tournaye H. et al. Embryo reduction in triplet pregnancies after assisted procreation: a comparative study. *Fertil Steril* 1993; 60: 504-509.
7. Callahan TL, Hall JE, Ettner SL et al. The economic impact of multiple-gestation pregnancies and the contribution of assisted-reproduction techniques to their incidence. *N Engl J Med* 1994 ;331:244-249
8. Cohen J, Jones HW. How to avoid multiple pregnancies in assistive reproductive technologies. *Semin in Reprod Med.* 2001; 19: 269-278
9. Evans MI, Berkowitz RL, Wapner RJ et al. Improvement in outcomes of multifetal pregnancy reduction with increased experience. *Am J Obstet Gynecol* 2001;184: 97-103
10. Fasouliotis SJ, Schenker JG. Multifetal pregnancy reduction: A review of the world results for the period 1993-1996. *Eur J Obstet Gynecol* 1997; 75: 183-190.
11. FIVNAT (French In vitro fertilisation registry: 1994). *Contracept Fertil Sex* 1995; 23: 490-493.
12. Gonen R, Heyman E, Asztalos EV et al. The outcome of triplet, quadriples, and quintuplet pregnancies managed in a perinatal unit. *Obstetric, Neonatal and follow-up Data.* *Am J Obstet Gynecol.* 1990; 2: 454-459.
13. Hanning R, Seifer D, Wheeler C et al. Effects on fetal number and multifetal reduction on length of IVF pregnancies. *Obstet Gynecol* 1996; 87: 694-697.
14. Leondires MP, Ernst SD, Miller BT, Scott RT Jr. Triplets: outcomes of expectant management versus multifetal reduction for 127 pregnancies. *Am J Obstet Gynecol* 2000;183:454-459
15. Newman RB, Hamwer C, Clinton -Miller M. Outpatient triplet management: A contemporary review. *Am J Obstet Gynecol* 1989; 161: 547-555.
16. US Department of Health and Human Services .Trends in twin and triplet births: 1980-1997. Washington, DC: Centers for Disease Control and Prevention; 1999.
17. Yaron Y, Bryant-Greenwood PK, Dave N et al. Multifetal pregnancy reductions of triplets to twins: comparison with nonreduced triplets and twins. *Am J Obstet Gynecol* 1999 ;180:1268-1271
18. Westergaard T, Wohlfart J, Aaby P et al. Population -based study of rate of multiple pregnancies in Denmark 1980-. *Br Med J* 1997; 314:775-779.