

# A single center experience with 1000 consecutive cases of multifetal pregnancy reduction

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**OBJECTIVE:** Multifetal pregnancy reduction (MPR) is a technique developed to reduce the risks of a multifetal pregnancy. The objective of this article was to report the outcome of MPR in the largest single-center experience to date.

**STUDY DESIGN:** A computerized database was used to determine the outcome of 1000 consecutive cases patients undergoing transabdominal MPR between the years 1986 and 1999. Outcomes analyzed included pregnancy loss rates, preterm delivery rates, and mean birth weights.

**RESULTS:** The complete pregnancy loss rate was 5.9%, whereas the unintended pregnancy loss rate was 5.4%. The loss rate was 9.5% in the first 200 cases and remained stable at 4.5% to 6.0% over the next 800 cases. The loss rate was lowest with starting numbers of two fetuses (2.5%), remained stable for three, four, and five fetuses, and increased to 12.9% with starting numbers of six fetuses or greater. Loss rates were similar with a finishing number of one or two (3.5% and 5.5%, respectively) but were highest for a finishing number of three (16.7%). Analysis of birth weights showed a linear decline with increasing starting and finishing numbers. Mean gestational age of delivery for finishing numbers of one, two, and three fetuses was 37.9, 35.3, and 33.5 weeks.

**CONCLUSION:** Unintended loss rates associated with MPR have stabilized at 5.4%. Loss rates are highest with starting numbers of six or more fetuses, but did not differ for starting numbers of three, four, or five fetuses. Gestational age of delivery for finishing numbers of one, two, and three fetuses are similar to that of nonreduced pregnancies. (Am J Obstet Gynecol 2002;187:1163-7.)

**Key words:** Multiple gestation, multifetal pregnancy reduction

Despite advances in reproductive endocrine techniques as well as efforts to limit the number of embryos transferred, the incidence of multiple births in the United States has continued to increase. Data from the National Center for Health Statistics indicate that from 1971-1977 to 1998, the twin rate increased from 1.8% to 2.8%, and the rate of triplets increased 5.9-fold, quadruplets 11.0-fold, and quintuplets 5.3-fold.<sup>1</sup> Similarly, the national trend toward an increase in preterm births (11.8% in 1999) is primarily the result of this increase in multiple births.

Multifetal pregnancy reduction (MPR) is a technique developed almost 15 years ago to decrease the incidence of preterm delivery in multiple gestations by reducing the number of live fetuses present in the uterus.<sup>2</sup> In the first report by our center, complete pregnancy loss rates associated with this procedure were 33%. In 1993 we reported

our experience with 200 completed cases of MPR, and the loss rate in that series had fallen to 9.5%.<sup>3</sup> In our expanded series of 400 cases of MPR, the complete pregnancy loss rate had decreased to 8%.<sup>4</sup> The improvement in outcomes with this procedure are thought to be largely due to increased operator experience as well as improvements in ultrasound equipment. Recently, Evans et al<sup>5</sup> published their fourth report on the international collaborative experience with MPR. That study, comprised of data on 3513 cases collected from 11 centers in five countries (including our center), also documented the continued improved outcome over time.

The purpose of this series of 1000 consecutive cases of MPR performed at a single center is to further assess the outcome of this procedure and to assess trends over time.

## Material and methods

A total of 1012 consecutive cases of MPR performed at the Mt Sinai Medical Center between the years of 1986 to 1999 constitute the study population. Because of the incomplete data in 12 cases, 1000 cases are included in this analysis, for a follow-up rate of 98.9%. All cases of MPR were performed for the indication of reducing fetal number. Cases in which a fetus was terminated because of a known anomaly (ie, selective termination) were not included in this analysis. All procedures were performed by

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**Table I.** Percentage of cases based on starting numbers divided into chronologic groups of 200

Starting No.	1-200	201-400	401-600	601-800	801-1000	Total
2	0	1.0	3.5	6.5	9.0	4.0
3	44.0	52.5	62.5	57.5	58.0	54.9
4	44.5	33.0	23.5	26.0	20.0	29.4
5	8.0	8.5	8.5	7.5	10.5	8.6
6+	3.5	5.0	2.0	2.5	2.5	3.1

**Table II.** Percentage of cases based on finishing numbers divided into chronologic groups of 200

Finishing No.	1-200	201-400	401-600	601-800	801-1000	Total
1	3.0	7.5	15.0	15.0	18.5	11.8
2	94.5	89.5	83.0	84.0	81.0	86.4
3	2.5	3.0	2.0	1.0	0.5	1.8

the transabdominal injection of potassium chloride into the region of the fetal thorax under ultrasound guidance and were performed by one of four operators (J. S., K. E., L. L., R. L. B.). Details relating to the technique of performing the procedure have been reported previously.<sup>3</sup> Since 1994, patients were offered chorionic villus sampling (CVS) before MPR, and outcomes for this group have been previously published.<sup>4</sup> Data on pregnancy outcome were collected in an ongoing fashion, and information entered into a specific MPR database with International Review Board approval.

Complete pregnancy loss was defined as loss of the entire pregnancy before 24 weeks' gestation. Unintended pregnancy loss was defined as the spontaneous, nonelective loss of the entire pregnancy before 24 weeks' gestation. Trends over time were analyzed by dividing cases into chronologic groups of 200. The gestational age (GA) at loss was evaluated by categorizing it into 4-week intervals after procedure. Mean GA of delivery was evaluated for the entire study population and by the starting and finishing numbers of fetuses. Rates of preterm births and mean birth weights were also assessed by the starting and finishing numbers.

Differences in proportions were evaluated by  $\chi^2$  test, Mantel-Haenszel  $\chi^2$  test for trend or two-tailed Fisher exact test as appropriate.

## Results

The number of MPRs annually performed at the Mt Sinai Medical Center has continued to increase, and 162 procedures were performed in the last year of the study. All procedures were performed between 9 and 13 weeks, with 85.8% being performed between 11.0 and 12.9 weeks. Tables I and II demonstrate trends in starting and finishing numbers over time. The majority of cases started with three or four fetuses (84.3%) and finished with two fetuses (86.4%). The proportion of cases start-

ing with triplets remained stable over time, whereas those starting with quadruplets decreased slightly. There is a trend toward an increase in cases starting with two fetuses and finishing with one. Elective reduction to a singleton was not offered until 1993, which corresponds to the 200 to 400 patient group in Table II.

Overall, 59 of the 1000 patients (5.9%) had a complete pregnancy loss before 24 weeks. Five of these cases were electively terminated, leaving an unintended loss rate of 5.4%. Indications for elective termination include hyperemesis, intrauterine growth restriction, oligohydramnios in two cases, and the death of a spouse. The loss rate in the initial 200 cases was 9.5%, and this fell to 6.0%, 5.0%, 4.5%, and 4.5% in the next 800 cases ( $P = .04$ , Fig 1).

Of the 54 unintended losses, only 8 (14.8%) occurred within 4 weeks of the procedure, whereas 30 (55.6%) were lost more than 8 weeks after MPR (Table III). There were no significant differences in loss rate based on GA at the time of the procedure ( $P = .8$ ).

The loss rate was lowest in patients starting with twins (2.5%) and highest for starting number of six or more (12.9%). There was a trend toward an increase in loss rates for starting number of six or more compared with starting numbers of two to five (12.9% vs 5.2%,  $P = .08$ ). There were no statistically significant differences in loss rates when comparing starting numbers of two, three, four, or five fetuses (Table IV).

The difference in loss rate for finishing numbers of one versus two (3.4% vs 5.5%) did not achieve statistical significance because of the relatively small number of reductions to a singleton. There was, however, a significant increase in loss rate (16.7%,  $P = .03$ ) for those finishing with triplets (Table V).

Of the 1000 cases, 941 (94.1%) were delivered at 24 or more weeks. Overall, the mean GA at delivery was 35.6 weeks (Table VI). The majority of patients (56.9%) were delivered at a GA of 36 or more weeks, and only 32

**Table III.** Gestational age at unintended pregnancy loss

Weeks after procedure	No. of losses (%)	Percent total
<4	8/54 (14.8%)	0.8
4-8	16/54 (29.6%)	1.6
>8	30/54 (55.6%)	3.0

**Table IV.** Unintended loss rate by starting number

Starting number (No.)	Unintended loss (%)
2 (40)	2.5
3 (549)	5.3
4 (294)	5.4
5 (86)	4.7
6+ (31)	12.9

**Table V.** Intended loss rate by finishing number

Finishing number (No.)	Loss rate (%)
1 (118)	3.4
2 (864)	5.5
3 (18)	16.7

\*  $P = .03$  for 1 or 2 vs 3

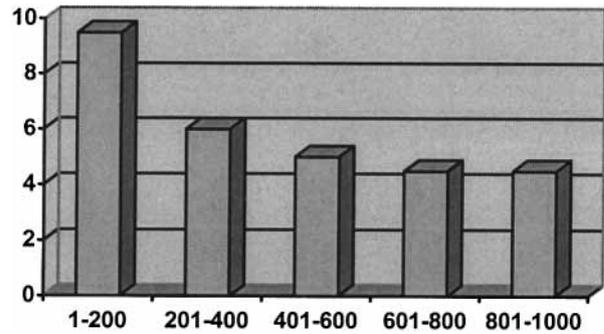
(3.4%) were delivered between 24 and 28 weeks. Interestingly, no significant differences in this very early prematurity rate was seen with the starting numbers of three, four, five, or six or more fetuses. The best outcome was seen for the small number of patients ( $n = 39$ ) starting with two fetuses. In this group, 92.3% delivered at 36 or more weeks.

Interestingly, although patients finishing with two or three fetuses were delivered on average at the same GA reported for nonreduced twins and triplets (ie, 35.3 and 33.5 weeks, respectively),<sup>10</sup> those finishing with one fetus were delivered approximately 2 weeks earlier than anticipated for nonreduced singletons (Table VII). No patients ending with a singleton was delivered before 28 weeks, and only 4.5% were delivered before 32 weeks. Only 3.9% of the patients reduced to twins were delivered before 28 weeks, and more than half (53.4%) were delivered at 36 weeks or later. As expected, 26.7% of patients finishing with triplets were delivered before 32 weeks.<sup>10</sup>

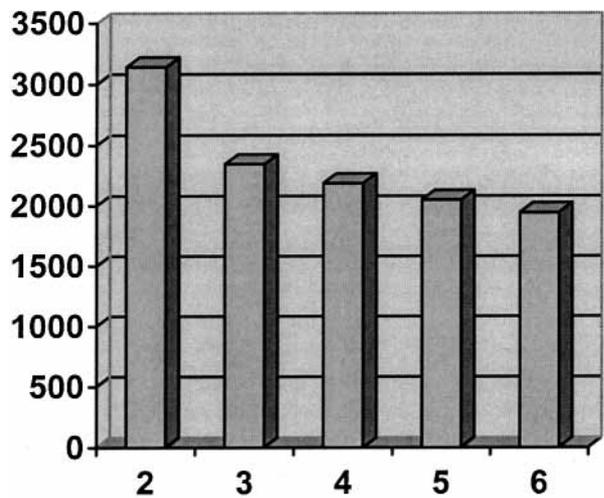
Analysis of mean birth weight by starting number of fetuses demonstrates a linear decline in birth weight with increasing starting numbers ( $P < .0001$ , Fig 2).

To eliminate the possible confounding effect of finishing number on starting number, mean birth weight was analyzed by starting number for only those patients reduced to twins, which confirmed a significant trend toward reduction in birth weight with increasing starting numbers ( $P < .0001$ ).

Fifteen patients underwent an unintended intrauterine demise of a single fetus after the MPR had been performed. The mean GA at demise in this group was 22.2



**Fig 1.** Unintended pregnancy loss rate over time. Cases are divided into chronologic groups of 200.



**Fig 2.** Mean birth weight (in grams) according to starting number of fetuses.

weeks, with a range of 15 to 28 weeks. In addition, three patients underwent subsequent selective termination of an abnormal fetus. There were 16 neonatal deaths, for a neonatal mortality rate of 0.9%. The majority of these deaths were due to severe prematurity, whereas two cases were attributed to birth asphyxia and a cardiac anomaly.

**Comment**

In this series of 1000 cases of MPR performed at a single institution, the number of procedures performed per year has continued to increase. Although the proportion of patients presenting with three fetuses has remained stable over time, we have seen a trend toward fewer quadruplets and more patients requesting a reduction from twins. Although the overwhelming majority of patients reduce to twins (86.4%), an increasing number are choosing reduce to a singleton. In the last 200 procedures reported in this series, almost 19% were reduced to a single fetus. Early in our experience a reduction to a singleton was only performed for medical indications, whereas later it was offered for purely elective indications.

**Table VI.** Gestational age at birth according to starting number

Starting No.	Mean (wk)	24-28 wk	28-32 wk	32-36 wk	36+ wk
2 (n = 39)	38.1	0 (0%)	1 (2.6%)	2 (5.1%)	36 (92.3%)
3 (n = 515)	35.8	16 (3.1%)	40 (7.8%)	153 (29.7%)	306 (59.4%)
4 (n = 278)	35.3	10 (3.6%)	28 (10.1%)	90 (32.4%)	150 (54.0%)
5 (n = 82)	34.7	5 (6.1%)	8 (9.8%)	36 (43.9%)	33 (40.2%)
6+ (n = 27)	34.6	1 (3.7%)	3 (11.1%)	13 (48.2%)	10 (37.0%)
Total (n = 941)	35.6	32 (3.4%)	80 (8.5%)	294 (31.2%)	535 (56.9%)

**Table VII.** Gestational age at birth according to finishing numbers

Finishing No.	Mean (wk)	24-28 wk	28-32 wk	32-36 wk	≥36 wk
1 (n = 111)	37.9	0 (0%)	5 (4.5%)	9 (8.1%)	97 (87.4%)
2 (n = 815)	35.3	32 (3.9%)	71 (8.7%)	277 (34.0%)	435 (53.4%)
3 (n = 15)	33.5	0 (0%)	4 (26.7%)	8 (53.3%)	3 (20.0%)

The overall unintended complete pregnancy loss rate of 5.4% is the lowest reported by our center to date. In our experience, the steepest portion of the learning curve seems to have occurred during the first 200 cases, when the loss rate was 9.5%. Since that time, the loss rate has only varied from 4.5% to 6.0%. This differs from data published in the international multicenter collaborative series of over 3500 cases of MPR from 11 different centers.<sup>6</sup> In that report, loss rates declined from 13.2% to 9.4% to 6.4% over a decade. This discrepancy may reflect the inherent differences of a multicenter experience versus that of a single center. The rapid learning curve at our institution is likely due to of the small number of operators performing the procedure as well as strict adherence to an established protocol. In addition, all procedures at our center were performed via the transabdominal approach, whereas the collaborative experience contains procedures performed transvaginally. This collaborative series documents a higher loss rate with transvaginal and transcervical procedures compared with those performed transabdominally (25.4% vs 8.5%,  $P < .0001$ ).<sup>6</sup>

It is interesting to consider that of the 5.4% of patients who underwent a complete pregnancy loss, more than half lost the pregnancy more than 2 months after the MPR procedure. Although it is nearly impossible to be certain whether those losses were due to the reduction procedure or are part of the background risk of pregnancy loss in this group, there are data to support the latter conclusion. Yaron et al<sup>9</sup> evaluated triplet-to-twin reductions at Wayne State University and compared them with two large sets of nonreduced twins. The loss rate among the approximately 800 sets of nonreduced twins was 5.8% and 6.3% for the two groups, which is very similar to their triplet-to-twin loss rate, as well as the loss rate in our series. Because the majority of our patients were reduced to twins, our overall loss rate is largely due to the

expected background losses. The loss rate of 0.8% in the first 4 weeks after procedure is similar to that associated with other needle-guided procedures (ie, amniocentesis, CVS) and may more accurately reflect the procedure-related risks of MPR. Furthermore, couples who consider the option of undergoing an MPR should also be aware of the background risk of pregnancy loss in nonreduced higher-order multiple gestations. The loss rate of 5.4% after MPR appears to be far less than that of nonreduced triplets. Data collected from 10 studies, including a total of 332 sets of nonreduced triplets, reported a complete pregnancy loss rate of 11%.<sup>10</sup>

This current series of 1000 cases confirms our previous finding that loss rates do not significantly differ based on starting numbers of two, three, four, or five fetuses.<sup>5</sup> There was, however, a trend toward a 2-fold increased risk of loss with starting numbers of six or more fetuses. This differs from data from the collaborative series, which reported higher loss rates with increasing starting numbers of fetuses. Similarly, although Evans et al<sup>6</sup> found that very premature delivery was correlated with the starting number, our data do not support this conclusion. The rate of very premature delivery was similar with starting numbers of three, four, five, or six or more fetuses and appeared to be lower in patients starting with twins.

Although loss rates did not vary with starting numbers of two to five fetuses, we did find a significant increase in loss rates with a finishing number of three. Because some patients with higher-order multiples are interested in reduction to triplets, this information needs to be incorporated into the counseling.

The overall mean GA of delivery in patients undergoing MPR was 35.6 weeks. Patients reduced to twins and triplets delivered at the same GA expected for nonreduced twins and triplets. Although this study does not provide a comparison group of nonreduced twins and

triplets, the literature suggests that nonreduced twins and triplets are delivered at approximately 35.5 and 33.5 weeks.<sup>9,10</sup> However, the mean GA of delivery of patients reduced to singletons was about 2 weeks earlier than that of nonreduced singletons.

Unlike our previous reports<sup>3,4</sup> but consistent with other published series,<sup>6-8</sup> birth weights were found to decrease with higher starting numbers. Although the exact pathophysiologic mechanisms underlying this phenomenon is uncertain, it has been suggested that there may be a fundamental "imprinting" of the uterus early in pregnancy that is not eliminated by an MPR.<sup>5</sup>

In conclusion, this large series confirms the low risk of pregnancy loss associated with MPR and demonstrates that patients undergoing this procedure behave similarly to their nonreduced counterparts, both in terms of pregnancy loss and GA at delivery. Although the overwhelming majority of our patients have reduced to twins, we have noted a trend toward more reductions to singletons. Unlike previous reports documenting higher risks with reduction to singletons, in our experience this is associated with the lowest loss rates and lowest chances of preterm delivery.<sup>6,11</sup> The increase in the elective reduction to a singleton seen in the last 200 cases may be due to the communication of this improved outcome to patients during initial consultation. Nevertheless, there are not enough data at this time to recommend that women opting for an MPR should be counseled to reduce to a singleton rather than twins.

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