



The Northwestern University Triplet Study II: Fourteen Triplet Pregnancies Delivered between 1981 and 1986

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Abstract. Fourteen triplet deliveries conducted between 1 January 1981 and 30 June 1986 at the principal teaching hospitals of Northwestern University Medical School are reviewed. Maternal demographic characteristics are listed, as are the obstetric outcomes, including mode of delivery, and the fetal outcome. The recent literature of triplet delivery is reviewed.

The rate of triplet delivery in our study was 0.37 per 1,000 live births. About two-thirds of the pregnancies resulted from the use of fertility-inducing agents. Ultrasonic confirmation was available in all cases. The majority of women were delivered by cesarean section (85%). No consistent pattern of presentation was seen. The mean weight of all 42 infants was 1,779 g (\pm 594). Unlike-sex triplets accounted for most of the sets (77%). The mean 5-min Apgar score of all infants was 9 and had no association with the order of deliveries. The weight differences by sex regardless of birth order were clinically insignificant. Neonatal mortality was 2.3%.

Key words: Triplets, Fertility drugs, Cesarean section, Birthweight, Neonatal mortality

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INTRODUCTION

Numerous factors contribute to clinical concern about triplet pregnancy. Central among these are the following: 1) the increasing use of fertility-inducing agents in the therapy of infertile women and the effects of these drugs on the incidence of multiple births, especially those of higher orders [44]; 2) the recent advances in neonatal care which have led to greatly improved chances for the survival of low birth-weight infants [21,36]; and 3) the need for more fertility-inducing agents as the numbers of infertile women increase in developed as well as developing countries [27].

During the past two decades, age-specific DZ twinning rates have declined in almost all developed nations [16]. It is possible that similar declines in the rate of triplet births have occurred in some (Japan, USA) [14,17] but not all (Australia) [3] countries which report these statistics. Since published clinical data generally are not recent (Japan 1980, USA 1962, Australia 1978, respectively), it is not possible to assess the secular trends of triplet births with reasonable certainty.

Review of national, regional and hospital reports of triplet data gives the impression that the body of clinical knowledge on this subject is small indeed. In all, there are 11 national surveys and 7 regional, local or hospital series [22]. Of the 7 clinical series [6-8,15,25,32,42], only one [7] deals with more than 100 sets of triplets, and this was a collective series from 150 hospitals. The other hospital series ranged from 4 [21] to 59 [15] sets of triplets.

This paper will review 14 sets of triplets delivered in two hospitals affiliated with Northwestern University Medical School in Chicago between the years 1981 and 1986. Prentice Women's Hospital and Maternity Center (PWHMC) and Evanston Hospital (EH) are part of a statewide referral network for the care of high-risk pregnancies. As such, patients with multiple gestations are referred for prenatal and intrapartum care. Both facilities utilize similar protocols for patient care and share the same resident physician staff. The care provided to high-risk patients is virtually identical in both institutions.

MATERIALS AND METHODS

PWHMC and EH are tertiary care centers. Parturients at both institutions represent, in general, the complex sociodemographic milieu of Chicago and its suburbs. In this study, 10 patients delivered at PWHMC and four at EH.

Data Collection

A data collection instrument was prepared to record antenatal, intrapartum and postpartum events. Information categories included: 1) maternal demographic and obstetric characteristics; 2) data pertaining to the method of delivery; and 3) infant outcome characteristics. Charts were obtained from a computer-generated list of triplet births at PWHMC and from a list derived from the personal records of the Chief of Perinatology (JH) at Evanston Hospital. All charts were reviewed by one individual (SA); coding questions were clarified by a senior member of the attending staff at PWHMC (LK). Full data pertaining to the perinatal outcomes of the newborns of these patients will be presented elsewhere [4]. Since this report is a descriptive analysis without comparisons of interventional treatments, no controls will be used.

RESULTS

During the five and a half year study period (1 January 1981 through 30 June 1986), 38,063 live births were recorded at both hospitals. Fourteen women were delivered of triplets for a rate of 0.37 per 1,000 live births or one woman delivered of triplets for every 2,719 puerperal women.

Mothers of Triplets

One woman had her labor induced prematurely because of hydrocephalus in one infant which did not respond to an attempt at selective fetocide. Although she was in the 23rd week of gestation, data from this pregnancy will not be analyzed along with that from the other pregnancies, as its inclusion would exert a bias on the remaining data for the average values for length of gestation, Apgar scores and mean weights.

Selected demographic and obstetric characteristics of the remaining 13 mothers are summarized in Table 1. The majority of the mothers (77%) were between 21-29 years of age. Thirteen puerpera were white; one was Hispanic. The preponderance of these gravida (62%) were delivered of their first pregnancy. Almost two-third had a prior history of infertility and required fertility-inducing agents to achieve their pregnancies.

Table 1 – Selected maternal demographic and obstetric characteristics

Patient no.	Age (yr)	Preg. hx.	Infert. treat.	Infert. drugs	Gest. age (weeks)	Tocolysis
1	34	10,000	+	Pergonal	35	
2	24	10,000	+	Clomid	29	Ritrodine
3	28	31,011	-		28	Ritrodine mg 50 ₄
4	25	10,000	+	Clomid	35	
5	26	10,000	-		30	Ritrodine mg 50 ₄
6	29	30,020	+	Pergonal	36	Ritrodine mg 50 ₄
7	29	20,010	+	Pergonal	37	
8	29	10,000	+	Clomid	36	
				Pergonal		
9	22	10,000	+	Pergonal	31	Ritrodine
10	22	20,010	-		30	Ritrodine mg 50 ₄
11	22	10,000	-		38	Ritrodine
12	32	20,010	+	Clomid	35	Ritrodine
13	18	10,000	-		30	Ritrodine mg 50 ₄

Ultrasonic confirmation of the existence of triplet pregnancy [39] and fetal growth occurred in all cases. More than half of the pregnancies were delivered at 35 or more weeks

of gestation. Tocolytic agents were administered to approximately two-thirds of the mothers. The length of stay in the hospital prior to delivery ranged from 0 to 48 days. Eight of the 13 gravida (61%) were hospitalized from 0 to 7 days. Similar proportions of the remainder (2 or 6.0%) were hospitalized for 7-14, 14-21 or more than 21 days, respectively. Only one mother had a prior multiple delivery (twins). In addition to preterm delivery (less than 35 weeks) in 10 patients, four (31%) experienced preeclampsia, and one mother each had an abruption or postpartum hemorrhage with atony.

Triplet Deliveries

Delivery characteristics are shown in Table 2. The majority of the women (11 or 85%)

Table 2 – Selected delivery characteristics

Patient no.	Days from adm. to del.	Method of delivery	Presentation			Placentation (fert. drug)	Placental wt. (combined, g)
			I	II	III		
1	2	CS (classic)	unknown			TT (+)	1500
2	2	CS (classic)	V	V	T	DT (+)	800
3	1	CS (low vert)	B	B	B	TT (-)	833
4	9	CS (low trans)	V	V	V	TT (+)	1445
5	6	CS (low vert)	V	V	B	TT (-)	997
6	26	CS (low trans)	V	B	B	DT (+)	1675
7	0	CS (low vert)	B	V	B	TT (+)	1430
8	1	A:MF B&C:BE	V	B	B	TT (+)	1250
9	17	CS	V	V	V	DT (+)	1134
10	1	CS	V	V	T	DT (-)	
11	19	CS (low vert)	V	V	B	TT (-)	1400
12	48	A:NSVD B:MF C:CS (low trans)	V	Brow	T	TT (+)	
13	8	CS (low vert)	V	B	B	unavail (N)	

MF = midforceps; BE = breech extraction

were delivered by primary cesarean section (CS). One woman had a section for the delivery of the third infant only. The preponderance of the placentas were described as being triamniotic-trichorionic upon pathologic examination. This form is more in common with maternities among black women [29]. The mean combined placental weight was $1,246 \pm 296$ g based on 10 cases in which this information was present. Of the 12 deliveries conducted by CS 4 were under general, 6 under epidural, 1 under spinal and 1 under a combination of epidural and general anesthesia, respectively. Cord gases were obtained at 12 of the 13 deliveries. The results of these examinations will be presented separately [5]. Fetal presentation was unrecorded in one instance only; no consistent pattern was seen in the others (Table 3).

Table 3 – Frequency of presentation combination

Triplet			No.	%
I	II	III		
V	B	B	3	23.08
V	V	V	2	15.38
V	V	V	2	15.38
V	V	B	2	15.38
B	B	B	1	7.69
B	V	B	1	7.69
V	B	T	2	15.38
Unknown			1	7.69
Total			13	100.00

Triplet Infants

Selected infant characteristics are shown in Table 4. The mean weight of all 42 infants was 1,779 ± 594 g. The mean weights of the infants by birth order were 1,803 ± 574 g, 1,883 ± 624 g and 1,666 ± 461 g, respectively. The mean weight of combined sets was 5,353 ± 1,555 g. Like-sex infants occurred in 3 (23%) of the maternities. Unlike-sex

Table 4 – Selected infant characteristics

Patient no.	Birth weight (g)			Combined weight	Sex by order of birth	Apgar 5-min			Survival		
	I	II	III			I	II	III	I	II	III
1	2890	2460	2540	7890	MFM	9	9	9	L	L	L
2	1330	1315	1210	3855	FMM	8	9	9	L	L	L
3	1120	1200	1150	3470	FMF	9	9	7	L	L	L
4	1565	2105	1690	5360	MMF	9	9	9	L	L	L
5	1520	1360	1420	4300	MFF	8	8	6	L	L	L
6	2470	2610	2150	7230	FMF	10	10	10	L	L	L
7	2540	3030	1830	7400	MMM	9	9	9	L	L	L
8	1960	2320	2400	6680	FMM	9	9	9	L	L	L
9	1560	1560	1520	4640	MFF	9	6	9	L	L	L
10	1200	1000	1400	3600	FFF	9	8	7	L	L	L
11	2067	2039	1840	5946	FFF	9	9	9	L	L	L
12	2045	2095	1550	5390	FMF	8	8	8	L	L	L
13	1180	1390	1270	3840	FMM	8	7	7	L	L	L
Mean	1803 ±579	1883 ±624	1666 ±461	5353.8 ±1555	like sex = 23 unlike sex = 77	9.5	8.9	8.7			

Mean of all (42) infants = 1779 ±594 g

triplets accounted for the remaining 10 sets (77%). The mean 5-min Apgar score of all infants was 9 and this number was not influenced by birth order. All of the infants were delivered alive.

Other Considerations

Table 5 shows sex composition of the sets and the frequency of the occurrence of each combination in relation to the mean birth weight of the set(s) with that combination. The influence of sex, birth weight and 5-min Apgar score regardless of birth order is shown in Table 6. The differences in the mean 5-min Apgar scores are clinically insignificant; the same is true for the weight differences by sex (regardless of birth order) ($P > 0.05$). The presence of one or more males within the triplet set did not appear to influence the length of gestation.

There is no consistent correlation between maternal age and the combined fetal weight. When the mean weight of the infants was examined in relation to order of birth, sex, and 5-min Apgar score (Table 7), males were heavier than females in those infants with low (1-7) or high (8-10) 5-min Apgar scores regardless of birth order. Table 8 shows the 5-min Apgar score by method of delivery and order of birth. Statistical evaluation of these data is impractical because of the small numbers. Table 9 shows the type of placenta by sex composition of triplet set.

Table 5 – Sex composition by mean weight of all sets with this combination

Sex combination	No. of sets	Mean birth weight, all sets, this combination (g)
MMM	1	7400
MFF	2	4470
MFM	1	7890
FMF	3	5363
FFF	2	4773
FMM	3	3843
MMF	1	5360

Table 6 – Mean birth weight and 5-min Apgar (mean) by order of birth and sex

Sex	Mean birth weight (mean 5-min Apgar)						Total		
	I	N	II	N	III	N	N	%	
M	2015 (8.8)	5	2008 (8.8)	8	1850 (8.6)	5	18	43	NS
F	1671 (8.8)	8	1684 (8.0)	5	1553 (8.2)	8	23	57	NS
M + F	1704 (8.1)	13	1779 (8.1)	13	1572 (7.9)	13	39	100	

Table 7 – Mean weight by 5-min Apgar scan by order of birth and infant sex

	Mean birth weight (g)					
	Apgar 0 (No.)		Apgar 1-7 (No.)		Apgar 8-10 (No.)	
	M	F	M	F	M	F
First baby	0	0	0	0	2015 (5)	1672 (8)
Second baby	0	0	1390 (1)	1560 (1)	2096 (7)	1715 (4)
Third baby	0	0	1270 (1)	1324 (3)	1995 (4)	1690 (5)

Table 8 – Five-minute Apgar score by method of delivery and order of birth

Method of delivery	Infants with Apgar 1-7	Infants with Apgar 8-10
<i>First baby</i>		
Vertex	0	2
Breech	0	0
CS	0	11
Subtotal	0	13
<i>Second baby</i>		
Vertex	0	1
Breech	0	1
CS	2	9
Subtotal	2	13
<i>Third baby</i>		
Vertex	0	0
Breech	0	1
CS	4	8
Subtotal	4	8
Total	6	35

Note: this table is an overview comparison between 5-min Apgar scores of infants with regard to presentation and order of delivery.

Table 9 – Placentation by sex composition of the triplet set

MMM	Sex of triplets			Total	Placental membrane	
	MMF	MFF	FFF		Chorionic	Amniotic
	2	2		4	Dichorionic	Diamniotic
1	3	3	1	8	Trichorionic	Triamniotic
	1			1	Not known	Triamniotic
1	6	5	1	13		

COMMENT

Experience with triplet pregnancies in two Chicago hospitals has been reviewed during a five and a half-year period between 1981 and mid-1986. We recognize that our high rate of triplet deliveries is artificial and based upon the hospitals' status as regional perinatal and endocrine centers. In terms of pregnancy wastage (stillbirth or death within the first 24 hours), the outcome was excellent. Only three of the 42 infants (7.1%) succumbed within the first 24 hours. This number compares favorably with the 6.6% overall pregnancy loss of twin gestations reported from the Chicago area in 1980 [21]. This figure also compares favorably with the 7.1% perinatal mortality rate in triplet gestations of 28 or more weeks as reported by Michlewitz [25]. Our neonatal mortality rate of 2.3% [4] compares very favorably with the 21% neonatal death rate reported by Syrop and Varner [42] in 1985 from the University of Iowa hospitals and clinics. This latter report, the largest published American review of triplets during the period under study, also contains an excellent review of recent obstetric literature pertaining to triplet gestation.

Ultrasound is not routinely used in our hospitals as it is in other institutions [23,34, 35,38,40]. However, all the women in this study had ultrasonic examination, for diagnosis and for assessment of fetal growth.

In one instance (Case no. 6, Tables 1-3), the use of ultrasound was followed by a diagnosis of combined anencephaly and hydrocephalus. The pregnancy was subsequently terminated (see above).

Although our study delineated the numbers of patients who were hospitalized prior to their delivery and the length of these hospitalizations, it did not evaluate the amount of bed rest obtained by each patient either prior to hospitalization or during her hospital stay. The value of bed rest in reducing the likelihood of onset of preterm uterine contractions is still a matter of controversy [10-12,18,21,26,36]. Part of this controversy relates to the difficulty in arriving at a consensus in the definition of bed rest. In addition, there is no consensus about the necessity to utilize control populations for comparison [1]. The early Swedish studies [36] describing the value of bed rest were longitudinal comparisons of outcome data of twins born to unrested mothers between 1963 and 1965 and rested mothers delivered between 1973 and 1978. All deliveries occurred at the same hospital. As these studies were uncontrolled, their importance has been questioned by some workers [30], but this criticism has not been and is not universal. Many clinicians rely on bed rest as a major part of antepartum management protocol [20,24,26,34]. The mechanism underlying the purported salutary effects of bed rest is not well understood. Among the possible considerations are improved uterine blood flow and, possibly, reduced intraabdominal pressure. A recent investigation by Schneider et al [41] on the relationship between premature contractions and maternal standing showed that uterine activity was markedly lessened when the mother was placed in the left recumbent position. Another study on ambulatory patients using a portable monitoring device documented that the frequency of uterine activity is significantly higher throughout pregnancy in twin gestations compared to singleton pregnancies [28]. A companion study by the same investigators showed that the frequency of contractions was significantly greater among women who subsequently developed preterm labor compared to that among women who labored at term [19].

A major deterrent to the more widespread implementation of institutionalized bed

rest is its cost, especially if bed rest is applied in hospitals in countries which do not have a scheme of socialized medicine to pay for these expenses. Few American reports have evaluated the cost of hospital bed rest. In one, Powers and Miller [37] calculated this cost to be \$ 6,000 per gravida between the 27th to 34th week of pregnancy. In their opinion, this expense was not justified in 1979 in the absence of documented efficacy in reducing the rate of prematurity, since the average cost for neonatal intensive care for the *surviving* twin infants in their study was only approximately \$ 1,700, taking into account *all* gestation periods. However, in the same study, the cost per survivor was computed for infants born at weeks 28-34; this cost was in excess of \$ 6,000 per infant [9].

The most extensive cost analyses of preterm births in multiple pregnancies have been the studies by Papiernik and coworkers [33,43]. These French investigations show that each twin pregnancy may cost as much as 10 times that of a singleton pregnancy. Under such circumstances there remains little doubt that any intervention that can effect even a small or modest decrease in the proportion of very low or low birth weight twin/triplets will have great social benefit. Unpublished observations from the institutions participating in the present study support this statement. At EH, patients with multiple gestation enrolled in one of the prepaid health plans (PruCare) have the benefit of a homemaker to relieve them of their household duties from the 28th week of pregnancy onwards. Because of this policy, reduction of physical activity is more easily attainable for these patients, and the outcomes of this intervention have been favorable [13]. At PWHMC, one of the private obstetricians insists that his patients with twin gestation reduce their physical activity and preferably go to bed after the 28th week of gestation. Compliance is enhanced by the physician's willingness to make house calls and conduct his antenatal examinations (including assessment of cervical effacement and dilatation) in the patient's home [31]. All triplet gestations reported in this study were put to bed at home or in hospital at 24 weeks and had weekly assessments of cervical status, but to date we have not attempted to quantify the extent of this "rest".

The majority of our study patients were delivered by CS in agreement with some but not all of the contemporary literature [7,15,25]. Favorable outcome cannot be guaranteed by CS [2], however, and vaginal delivery is not always associated with poor outcome. Some clinicians are of the opinion that CS is indicated because it obviates the necessity of delivering a high percentage of fetuses with malpresentation. According to Itzkowic [15], it is reasonable to allow vaginal delivery after 34 weeks of gestation in uncomplicated triplet gestations. (The author does not define the word *uncomplicated*). The merits of CS notwithstanding, one of the authors of this study (LK) has delivered two sets of term triplets vaginally with no anesthesia other than pudendal block.

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