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Multicentric Multiple Pregnancy Study III: Triplets

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Abstract

Objective: The aim of the study is to evaluate demographic and clinical characteristics of triplet pregnancies and to compare with those of twins.

Methods: The prevalence of triplets was found as 0.97/1000 and the ratio of them within multiple pregnancies was determined as 4.9%. At least one fetus died in the antenatal period or at birth at ratio of 32.43% in triplets. Perinatal mortality ratio was 234.2 per thousand in triplets. Perinatal mortality was high in cases born before 29th gestational week, and less than 1000 g.

Results: Demographic data related to the triplets delivered between the period of 2003 and 2004, including mean maternal age, parity, fetal and perinatal mortality, gestational week at delivery, mode of delivery and maternal morbidity, fetal or newborn's weight and sex were determined from the questionnaire forms and data obtained from 15 obstetrics centers. They were compared with those of twins. Chi-square, Fischer's exact and Student's t tests are used for statistical analyses.

Conclusion: Assisted reproduction techniques increased high order multiple pregnancies causing high fetal morbidity and mortality and requiring perinatal center care.

Keywords: Triplet, perinatal mortality, multicentric study.

Çok merkezli çoğul gebelik çalışması III - üçüz gebelikler

Amaç: Bu çalışmada ülkemizdeki çoğul gebelikler içinde saptanan üçüz gebeliklerin demografik ve klinik özellikleri saptanarak, ikizler ile karşılaştırıldı.

Yöntem: 2003-2004 yıllarındaki çoğul gebelikler içindeki üçüzlerde anne yaşı, gebelik ve doğum sayıları, doğum haftası ve şekli, yenidoğan ağırlıkları, cinsiyetler ile fetus ve yenidoğan mortalitesi ile anne morbiditesi gibi demografik veriler araştırıldı, ikizler ile karşılaştırıldı. Veriler onbeş farklı Kadın Hastalıkları ve Doğum Kliniğinin anket ve veri formları yardımı ile elde edildi. İstatistiksel yöntem olarak Chi-square, Fisher's exact ve Student t testleri kullanıldı.

Bulgular: Üçüzlerin prevalansı 0.97/1000 ve çoğul gebelikler içindeki oranı %4.9 olarak bulundu. Üçüzlerin %32.43'ünde gebelikte en az bir fetusun antenatal dönemde veya doğumda kaybedilmiş olduğu, perinatal mortalite oranının binde 234.2 olduğu belirlendi. Gebeliğin 29. haftasından önce veya 1000 g altında doğanlarda, perinatal mortalite daha yüksek oranda bulundu.

Sonuç: Yardımla üreme tekniklerinin kullanımı sonucunda üçüz gebelikler artmaktadır. Bu durum yüksek perinatal mortalite ve morbiditeye sahip olduğundan perinatal merkezlerde takibi gerektirmektedir.

Anahtar Sözcükler: Üçüz, perinatal mortalite, çok merkezli çalışma.

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Introduction

With the introduction of artificial reproduction techniques (ART), the ratio of pregnant women has increased within the last 20 years in our country. The success of centers using induction of ovulation, in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) is measured by the ratio of pregnancy, meanwhile, the real measure, the healthy fetus at term (favorably singleton) is sometimes ignored.

Because of the reduced pregnancy rates by the conservative approaches in the favor of Singleton pregnancies and the psychological stress brought by failed pregnancy after a long and expensive treatment processes and to prevent the decrease in the success of the Assisted Reproductive Technique (ART) centers, implementation of aggressive therapies which may result multiple pregnancies are preferred physicians as well as by the patients, though well-known complications. This is accompanied by a higher number of twin and multiple pregnancy rates. Triplet pregnancy rates, once one per ten thousand,[1] has increased up to seven per ten thousand in recent years.[2]

As known, multiple pregnancies are responsible for 10% of perinatal mortality.[3] In triplet pregnancy perinatal mortality rate is 9 times as much as those of Singleton pregnancies and twice as much in twins.[3] The main factor related to this ratio is the presence of premature birth.[4] The aim of this cross-sectional multi-center study was to reveal the basic epidemiological parameters and mortality ratios in the triplet pregnancies seen in various Obstetrics and Gynecology clinics in our country.

Methods

This study, covering the years 2003-2004, has been performed with the help of survey and clinical information forms sent to the 15 Gynecology and Obstetrics Clinics of University Hospitals and the Training and Research Hospitals in various regions of Turkey. Maternal age, number of pregnancies and births, the number of fetuses, gestational age, birth type, birth weight, gender, mortality and maternal mortality-morbidity parameters were investigated in the survey. Some unreported data in the survey were re-questioned and the missing ones were completed. The data of multiple pregnancy ones with mortality in the perinatal period was compared to those without mortality using statistical tests of chi-square, Fisher's exact and Student's t-test.

The term “stillbirth” has been defined for the death of the fetus, who (or any of his twins) is at least 400 grams of weight or who completed 20 th gestational week, before birth or no respiration after birth or no heart beat. The term “early neonatal death” has been defined for neonatal deaths within the first 7 days after birth. Only ovulation induction, ICSI and IVF pregnancies have been accepted as assisted reproductive techniques.

Results

Nine of the fifteen centers included in the study were University Hospitals and the rest were Training and Research Hospitals. Though all centers completed the first survey data forms, only ten centers completed both parts.

The total number of births in 15 centers participating in the study in 2003-2004 was 70,091; 1310 of them were twins and 53 of them were triplets. Accordingly, the prevalence of twin birth was 18.6/1000 and the prevalence of triplet birth was 0.75/1000. According to 10 centers who provided detailed results, the total number of births was 43.258; 818 of them were twins (18.9/1000) and 42 of them were triplets (0.97/1000). The ratio of triplet pregnancies in the multiple pregnancies was found to be 4.9%. Comparative demographic data of total of 829 multiple pregnancies (792 twins and 37 triplets), assessed after removing those with

Table 1. Demographic and clinical data in multiple pregnancies.

	Twins (n:792)	Triplets (n:37)	p
Age (Mean ±SD)	27.91±5.36	28.76±4.23	0.346
Number of pregnancies (Mean± SD	2.40±1.90	2.20±2.41	0.555
Number of biths (Mean± SD))	1.10±1.66	0.97±2.19	0.670
Number of biths (Mean± SD)	34.33±3.52	30.65±3.35	**0.000**
Fetal neonatal weight (grams) (Mean± SD)	2167±638	1443±526	**0.000**

missing, are shown in Table 1. The birth week and the neonatal weight of triplets were found to be statistically different than the ones of twins (p <0.000).

Perinatal mortality rate in twin pregnancies was 106.9 per thousand (136/1272) and perinatal mortality rate in triplets was 234.2 per thousand (26/111) and the difference was more than 2-fold (Table 2). At least one fetus loss was present in 14% of twin pregnancies and 32% of triplet pregnancies (Table 2). The chance of pregnancy without fetal loss was 85% in twins and 67% in triplets. In triplet pregnancies, death rate in male fetuses was 31% and death rate in female fetuses was 33%. The loss of all fetuses in the multiple pregnancies was found to be 7.58%.

With the assessment of multiple pregnancies for mortality, it was found that fetus(es) with lower weight died in 78% (35/45) of twins and in 75% (6/8) of triplets. In these pregnancies in which at least one fetus was alive, the rate of cesarean section was 64% in twins and 100% in triplets. The comparison of demographic and clinical data of triplet pregnancies with and without mortality is shown in Table 3.

When evaluated for premature birth, available data has shown that 44% of twins and 87% of triplets was born at 34th week or earlier. The probability of giving birth of triplet pregnancies at 24th, 28th and 34th weeks were found to be twice, thrice and twice higher than the one in twin pregnancies at respective weeks.

When the perinatal mortality in triplet pregnancies is evaluated acording to the parity, the mortality ratio was 333 (7/21) per thousand in primigravida and 286 (4/14) per thousand in multigravida. The difference was not statistically significant (p >0.05). However, double and triple losses were more frequently observed in primigravida, single losses were more in multigravida. When the mortality in triplet pregnancies is evaluated according to the gestational week, it is seen that loss of all fetuses occured before 29 weeks of gestation. Especially under the 29 weeks of gestation this high mortality rate was statistically significant (p<0.001) and the mortality rate decreased with ongoing gestational weeks (p <0.05). However, there was no change

Table 2. Perinatal mortality in multiple pregnancies (673 cases with data).

	Twins (n:636)	Triplets (n:37)	Total (n:673)
All deceased	45 (%7.07)	6 (%16.21)	51 (% 7.58)
One alive	46 (%7.23)	2 (% 5.40)	48 (% 7.13)
Two of them alive	545 (%85.69)	4 (%10.81)	549 (%81.57)
Three of them alive	-	25 (%67.56)	25 (%3.71)
At least one deceased	91 (%14.30)	12 (%32.43)	103 (%15.30)

Table 3. The comparison of demographic and clinical data of triplet pregnancies with and without mortality (n: 37) (Values are shown as Mean ± Standard deviation).

	One deceased (n:4)	Two deceased (n:2)	Three deceased (n:6)	Any deceased (n:12)	All three alive (n:25)	P
Age	28.50±4.79	30.50±3.19	28.67±3.00	28.92±4.32	28.68±4.27	>0.05
Gestation	1.75±0.50	1.00±0.00	1.20±0.44	1.36±0.50	2.58±2.83	<0.05
Parity	0.80±0.50		0.20±0.40	0.40±0.50	1.26±2.61	>0.05
Birth Week	30.75±3.30	31.50±3.50	25.67±2.07	28.33±3.70	31.76±2.55	**<0.001**
Weight	1417±494 g	1640±167 g	711±205 g	1101±513 g	1606±482 g	**<0.001**
Weight of live fetus	1426±457 g	1655±219 g	-	1472±421 g	1606±482 g	>0.05
Weight of dead fetus	1400±637 g	1633±274 g	711±205 g	959±478 g	-	-
Primigravida	_	2/2	5/6	8/12	15/25	>0.05
Cesarian Section	4/4 (%100)	2/2 (%100)	1/6 (%17)	7/12 (%58)	23/25 (%92)	**<0.001**

Table 4. The comparison of triplet pregnancies with and without mortality according to the gestational week (n: 37).

	One deceased (n:4)	Two deceased (n:2)	Three deceased (n:6)	Any deceased (n:12)	All three alive (n:25)	P
< 29 weeks	-	-	6	6	3	**<0.001**
29-32 week	2	1	-	3	9	>0.05
> 32 week	2	1	-	3	13	>0.05

in the probability of pregnancy without any loss (Table 4). Survival rate in triplet pregnancies is shown in the Table 5 and survival graph (Figure 1). When the perinatal mortality in triplet pregnancies is evaluated according to the birth weight, the mortality ratio was 76% (19/21) in babies born with a birth weight of 1000 grams or lesser and the ratio was 7.7% (7/90) in babies

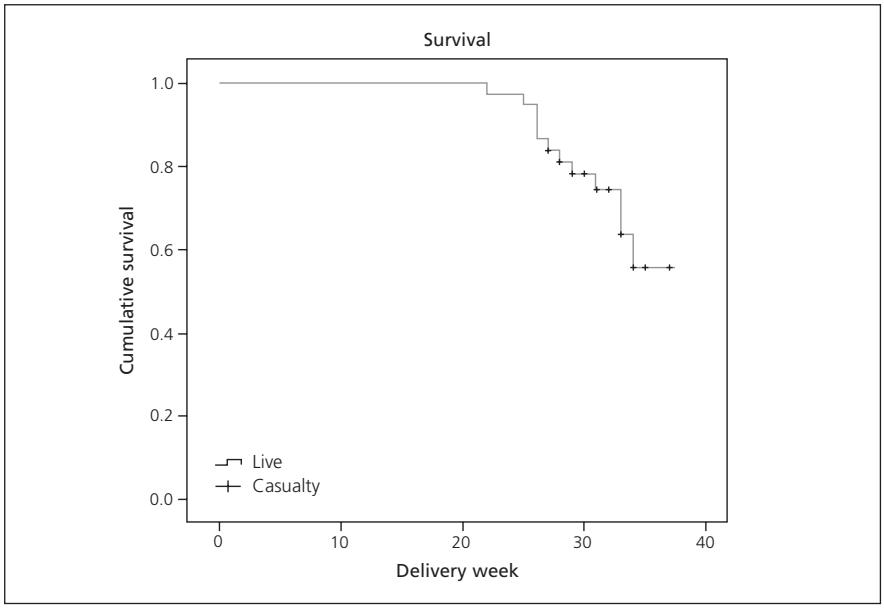

Figure 1. Survival graphic in triplets.

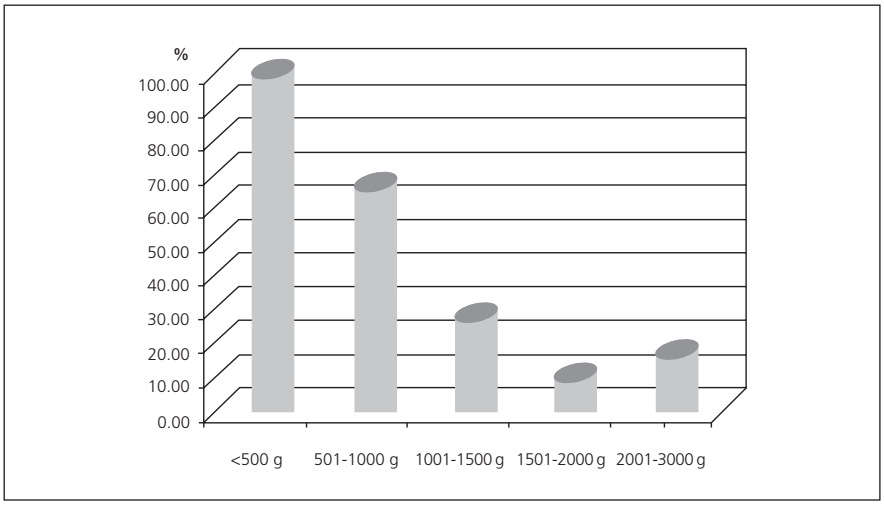

Figure 2. Mortality ratios in triplet pregnancies according to birth weight

Table 5. The ratio of living fetuses in triplet pregnancies according to the gestational week.

Gestational Week	Living Fetus (%)
20-24 Weeks	97
25-27 Weeks	84
28-30 Weeks	78
31-33 Weeks	70
34-36 Weeks	68
> 36 Weeks	68

born with a birth weight more than 1000 grams. The difference was statistically significant (p <0.001). However, there was no statistical difference between rates of pregnancy without loss (Table 6). Table 7 and Figure 2 shows mortality rates according to the weight of fetuses.

When the perinatal mortality in triplet pregnancies is evaluated according to the gender, it was seen that 24.19% of male fetuses (15/62)

Table 6. The comparison of triplet pregnancies with and without mortality according to the birth weight (n: 37).

	One deceased (n:4)	Two deceased (n:2)	Three deceased (n:6)	Any deceased (n:12)	All three alive (n:25)	P
≤ 1000 g	1/3	-	18/18	19/21	6/75	<0.001
1001-2000	2/7	4/6	-	6/13	53/75	>0.05
>2000	_	-	-	_	16/75	>0.05

Table 7. The relation of fetal-neonatal mortality with birth weight.

	Fetal-neonatal mortality (+)	Fetal-neonatal mortality (-)	Total	Mortality %
< 500 g	1	-	1	100
501-1000 g	6	3	9	66,7
1001-1500 g	3	8	11	27,3
1501-2000 g	1	9	10	10,0
2001-3000 g	1	5	6	16,7
> 3000	-	-	-	-
Total	12	25	37	

and 22.44% (11/49) of female fetuses died. But, the difference was not statistically significant (p >0.05). When the maternal morbidity in triplet pregnancies was assessed, though data is inadequate, available data showed that some treatment was managed for premature birth and the caesarian section ratio was 93% in case of living fetuses.

Discussion

The main reasons of high perinatal mortality rate in multiple pregnancies are the premature births and complications related to it such as respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage. Fetal malformations, intrauterine inappropriate and complications related to the placenta are the other reasons.[4]

In our country, antenatal and neonatal care services could not keep pace with the advances in the reproductive technologies.[5] Therefore, specialist and minor associations and the Ministry of Health, as well, involved in a quest. Indeed, their results were seen in recent years, and the number of embryos transferred in IVF programs was limited with a regulation.[6]

Concerning the triplet pregnancy outcomes in some centers in our country, our study found the prevalence of triplets as 9.7 per ten thousand. Probability of premature birth was 87%, perinatal mortality was 234.2 per thousand and the ratio of pregnant women losing any fetus in the antenatal period or birth was 32% and the ratio of pregnant women losing all fetuses was 16.21%. Clinical studies reported from Turkey, the ratio triplets in multiple pregnancies were reported within the range of 3-26% and their mortality rate was reported % in the range of 3.5-37%.[7-11] Our ratio of triplets approximating 4% is in accordance with the ratios of other studies. In our series, 32% loss rate is suggested to be related to the inclusion of ones with small gestational ages.

Ulug et al reported the mean birth week as 33.4 weeks, mean birth weight as 1824 grams and the mortality rate as 5% in the series of 55 viable triplet pregnancies.[12] The results of our study are different as our study also covered the results of those previable. The neonatal mortality in the triplets in our study is highest in the births before 29 weeks of gestation at birth is highest. The mean birth week in the triplet pregnancies with mortality (28.33±3.70), was approximately 3.4 weeks earlier than the ones without mortality (31.76±2.55). When the losses in the triplets were examined, the survival chance of births before 29 weeks was the lowest. The ratio of one loss was 10.81%, the ratio of two losses was 5:40% and the ratio of three losses was 16.21%. Overall perinatal mortality was 324 per thousand in triplets. This ratio was found as 370 per thousand in the study of Yayla et al.[11] When compared with the singleton pregnancies, birth weights of twins are 25% lesser, birth weights of triplets are 50% lesser and the birth weights of quadruplets or more multiple pregnancies are 70% lesser.[1] In multiple pregnancies, the fetus died, was the one with lower weight in about three quarters. The living fetus with a lost twin was 770 grams heavier than the lost one but was 325 grams lighter than those both born alive. This may be due to born of normal fetus immediately after death of twin or continuing growth of the other fetus after the death of twin. Similar to twins, in triplets the loss of fetuses was more in fetuses with a weight lower than 1000 grams.

The discordant development between twins has been suggested (discordance) as an important factor affecting mortality in twins and poorer prognosis was reported in the discordant twins even in the absence of twin-twin transfusion syndrome or congenital anomaly.[13] A similar situation may also apply to the triplets.

In our study, mortality in those born before 25 weeks or 500 grams of birth weight was 100%, while the pregnancy progresses, mortali-

ty has dropped to 10%. 29 weeks gestational week and weight limit of 1000 grams are comforting parameters in the follow up.

Although the limited data to make comparison in terms of maternal morbidity, there was a need of treatment for premature birth in one of two triplet pregnancies and cesarean section rate was over 90%.

Conclusion

In our study, the rate of multiple pregnancies with more than two fetuses was approximating one per thousand; this is 6-10 times higher than expected. Though perinatal mortality in triplet pregnancies was associated with gestational week and birth weight, chance for all fetuses to live showed no difference according to the gestational week and birth weight. This suggests that triplet pregnancies are prone to increase perinatal mortality. Therefore, prevention of multiple pregnancies with more than two fetuses may help reducing perinatal mortality.

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