

Multicentric Multiple Pregnancy Study II: Perinatal Mortality in Twins

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Abstract

Objective: The aim of the study is to determine the relationship between perinatal mortality and clinical demographic characteristics in twin pregnancies.

Methods: A questionnaire and data obtained from 15 obstetrics centers was used to show the relationship between perinatal mortality and maternal age, parity, maternal morbidity, gestational week at delivery, mode of delivery, fetal or newborn's weight and sex in twin pregnancies, delivered between the period of 2003 and 2004. Chi-square, Fischer's exact and Student's t tests are used for statistical analyses.

Results: Perinatal mortality ratio was 107 per thousand in twins. A chance of delivery without fetal or neonatal mortality was assessed in 85% of the twin pregnancies. Mortality was high in cases born before 30th gestational week, and less than 1000g, also in twins with the same sex, in females, in discordant for growth and in small ones.

Conclusion: According to the results of 15 different national obstetrics centers, mortality is found in 15% of the twin pregnancies at least in one of the twin pairs. Perinatal mortality ratio is 107 per thousand. Discordant females born before the 30th gestational week have the highest risk.

Keywords: Twin pregnancy, perinatal mortality, multicentric study.

Çok merkezli çoğul gebelik çalışması II: ikizlerde perinatal mortalite

Amaç: Çalışmanın amacı ülkemizdeki ikiz gebeliklerde perinatal mortalite oranını ve bu oranın klinik bulgular ile ilişkisini araştırmak.

Yöntem: Onbeş değişik Kadın Hastalıkları ve Doğum Kliniğinden elde edilen anket ve veri formlarının yardımı ile 2003-2004 yıllarındaki ikiz gebeliklerde perinatal mortalite ile anne yaşı, gebelik ve doğum sayıları, anne morbiditesi, doğum haftası ve şekli, yenidoğan ağırlığı ve cinsiyeti arasındaki ilişki araştırıldı. İstatistiksel yöntem olarak Chi-square, Fisher's exact ve Student t testleri kullanıldı.

Bulgular: İkizlerde perinatal mortalite binde 107, ikiz gebeliklerde kayıpsız doğum şansı %85 olarak belirlendi. Gebeliğin 30. haftasından önce veya 1000 g'ın altında doğanlarda, aynı cinsiyetteki ikizlerde, kızlarda, uyumsuz gelişen ve küçük olan ikiz eşlerinde mortalite daha yüksek oranda bulundu.

Sonuç: Ülkemizdeki onbeş ayrı merkezimizin verilerine göre ikiz gebeliklerin %15'inde bir veya her iki ikiz eşini de ilgilendiren kayıp söz konusudur ve perinatal mortalite oranı binde 107'dir. Gebeliğin 30 haftasından önce doğan uyumsuz kız ikizler en yüksek riske sahip olan gruptur.

Anahtar Sözcükler: İkiz gebelik, perinatal mortalite, çok merkezli çalışma.

Introduction

According to the general result of all studies in the world, multiple pregnancies are responsible for approximately 10% of perinatal deaths. Similarly, 8% of fetal deaths and 14% of neonatal deaths are related with multiple pregnancies. When compared to single pregnancies, perinatal mortality rate is four times higher in twin pregnancies and nine times higher in triplet and above pregnancies.¹ For example, monozygotic monochorionic twins are the group under the highest risk depending on cell division causing chromosomal or other lethal formations. Again, abnormal placenta exchanges and improper growth in fetuses among complications peculiar to monochorionic twins cause increase in morbidity and mortality.^{1,3}

Though it has been expressed in many scientific meetings that there is an increase in multiple pregnancies recently in Turkey, no study has been performed for factors affecting multiple pregnancy rates, maternal and fetal morbidity and mortality related with multiple pregnancies. The widest research including many centers on this subject was published by current study group.⁴

Our goal in this multicentric cross-sectional study is to present perinatal mortality rates of twin pregnancies in some centers in our country and some basic epidemiological parameters which may be related with them.

Methods

This study was done by questionnaire and clinical information forms sent to 15 different clinics of obstetrics and gynecology within universities and training research hospitals around Turkey between 2003 and 2004. Maternal age, gestation and delivery counts, conception type, delivery week and type, newborn weight and

gender and mortality, and maternal mortality-morbidity parameters were questioned in the questionnaire. Some data not reported in the questionnaire form were questioned again and missing data were completed. Data in the group where mortality was detected in perinatal period (deliveries over 20th gestational week and first week after delivery) was compared with data in multiple pregnancy group without mortality by applying Chi square, Fisher's exact and Student T tests. $p < 0.05$ was taken as a statistical significance limit.

Stillbirth was accepted as the death of fetuses who completed 20th gestational week and are at least 400gr before delivery or being unable to breath after delivery or having no heart beating while early neonatal death was accepted as newborn deaths within first 7 days after delivery; incompatible twin development was accepted as 20% difference between weights of newborns.

Results

Total deliveries of 15 centers included into the study were 70.091 between 2003 and 2004, and 1310 of them were twins. According to this, twin delivery prevalence was found as 18.6 per thousand. Twins constituted 96% of multiple pregnancies. Delivery number of 10 centers who sent detailed twin data was 43258 and 818 of them were twin and it is suitable to the general rate (18.6 per thousand). Among them, 792 twin pregnancies formed the perinatal mortality study group since 26 cases had insufficient data. Demographical data of this group was shown in Table 1.

In multiple pregnancies, the risk of losing all pregnancy products was found as 7.07% (Table 2). In twin pregnancies, perinatal mortality rate was 106.9 per thousand (136/1272). There was one or more fetus-newborn loss in 14.3% of

twin pregnancies (Table 2). The chance of twin pregnancy without loss was 85.7%.

The weight of living one in twins with one lost was found averagely 782g higher than still-born and 325g less than the mean birth weight of those both born alive. Mean weight of dead fetus in those with single loss was 355g higher than those with double loss (Table 3). Cesarean operation was mostly applied to twins who were both alive.

It was observed that prognosis was bad if delivery week for pregnant were under week 28, and that mortality decreased significantly when delivery week was above 30th week ($p<0.001$) (Table 4) (Figure 1).

In twins, surviving chance of fetuses over 1000 g was statistically higher than those below 1000g with a significant rate ($p<0.001$). Mortality rate of those with 1001-1500g weight was 20%. Mortality rate decreased to 7% in those with 1500g newborn weight and to 1.7% in those with over 2000g newborn weight (Table 5) (Figure 2).

When gender and weight ranges of twins were analyzed generally, it was seen that mean birth weight of boys (2243 ± 673 g) was higher than girls (2089 ± 666 g). When we analyzed the

Table 1. Demographical and clinical data of twin pregnancies in the study group.

	Twin (n: 792)
Age	27.91 \pm 5.36
Pregnancy number	2.40 \pm 1.90
Pregnancy week	1.10 \pm 1.66
Delivery week	34.41 \pm 3.28
Fetal neonatal weight	2172 \pm 674 g

Values are expressed as Mean \pm Standard Deviation.

Table 2. Perinatal mortality in twin pregnancies.

	Twin (n: 636)
All lost	45 (7.07%)
One is alive	46 (7.23%)
Both alive	545 (85.69%)
At least one lost	91 (14.30%)

association between mortality and gender, we found that mortality was 14% in girls (82/582) while it was 8.5% in boys (55/650) ($p<0.01$). Mortality rate was found 22% in girl/girl twins (42/192), 12% in boy/boy twins (28/227), and 11% in mixed twins (21/197). Increased mortality in girl/girl twins was found statistically significant ($p<0.01$). Mortality risk in twins with same gender (70/419: 17%) was higher than twins with different gender (27/203: 13%) ($p<0.05$) (Table 6).

Table 3. Comparison of groups with and without perinatal mortality in twins (n:636).

	Single mortality (d)	Double mortality (n: 46)	At least one mortality (n: 91)	No mortality (n: 545)	p
Age	27.30 \pm 5.32	26.84 \pm 5.26	27.07 \pm 5.26	28.07 \pm 5.44	>0.05
Gestation	2.71 \pm 1.92	2.62 \pm 2.24	2.67 \pm 2.06	2.39 \pm 1.92	>0.05
Parity	1.26 \pm 1.74	1.00 \pm 1.54	1.14 \pm 1.64	1.09 \pm 1.72	>0.05
Delivery week	32.57 \pm 4.03	26.89 \pm 3.62	29.66 \pm 4.78	35.07 \pm 2.56	<0.001
Cesarean	29/45 (64%)	10/46 (22%)	39/91 (43%)	398/545 (73%)	<0.001
Weight of surviving one	1972 \pm 807g	–	1972 \pm 807g	2297 \pm 539g	<0.01
Weight of lost one	1201 \pm 615g	846 \pm 462g	1190 \pm 782g	–	<0.01
P	<0.001	–	<0.001	–	

Values are expressed as Mean \pm Standard Deviation.

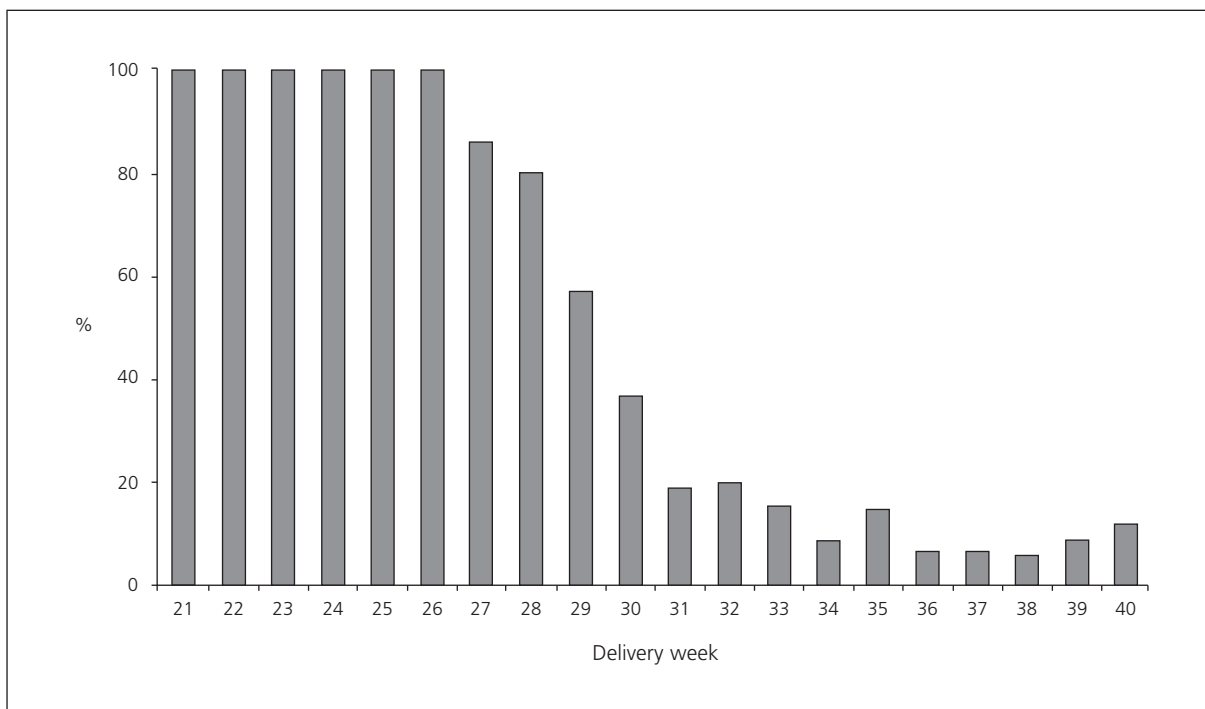


Figure 1. Delivery week and mortality in twins (%).

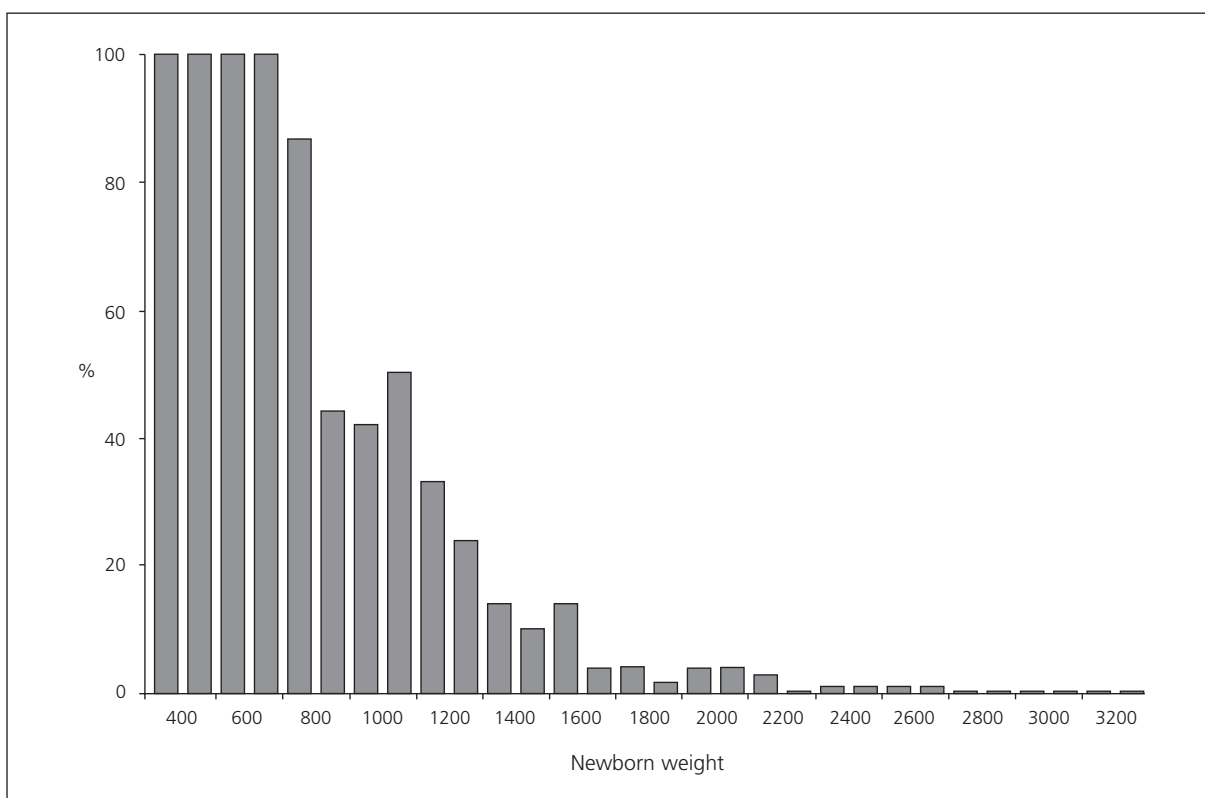


Figure 2. Newborn weight (g) and mortality (%) in twins.

Table 4. The relation of perinatal morbidity with gestational week in twin pregnancies (n:636)..

	No mortality	≥Mortality Exists	Total	Mortality (%)
Week 20-24	0	14	14	100
Week 25-27	2	23	25	92.0
Week 28-30	30	17	47	36.2
Week 30-31	128	15	143	10.5
Week 34-36	206	15	221	6.8
Week >36	176	9	185	4.9
Total	545	91	636	14

Table 5. The relation of perinatal morbidity with birth weight in twins (n:636x2=1272).

	No mortality	Mortality Exists	Total	Mortality (%)
Week 20-24	0	18	18	100
Week 25-27	21	65	86	75.6
Week 28-30	89	23	112	20.5
Week 30-31	252	19	271	7.0
Week 34-36	681	12	693	1.7
Week >36	92	0	92	0
Total	1135	137	1272	10.8

Table 6. Relationship between gender and mortality in twins with known gender (n:616) (Girl: 582; Boy: 650).

	Single mortality (n: 45x2)	Double mortality (n: 46x2)	At least one mortality (n: 91x2)	No mortality (n: 525x2)	Total 1232
Dead girl	23	59	82	–	82
Dead boy	22	33	55	–	55
Living girl	23	–	23	477	500
Living boy	22	–	22	573	595
Girl + girl	15 single	27 double	42	150	192
Boy + Boy	14 single	14 double	28	199	227
Girl + Boy	16 single	5 double	21	176	197
Total	90	92	192	1050	1232

When twin pregnancies which have at least one living fetus were analyzed, it was found that younger fetus was lost in 78% (35/45) of them. 51.64% (47/91) of twins with perinatal loss were discordant twins. Discordant twin rate in the group without loss was 21.28% (116/545). When discordant twins were examined in terms of mortality, 64% of losses occurred in younger one of twin. Mortality of

28.83% in discordant twin pregnancies was statistically and significantly three times higher than mortality of 9.30% in concordant twin pregnancies ($p<0.001$) (Table 7).

When the relationship between mortality and antenatal maternal disease in twins was evaluated, it was seen that hypertensive problems (preeclampsia, eclampsia), early membrane rupture and systemic diseases (diabetes,

Table 7. Discordance and perinatal mortality in twins.

	Younger twin mortality	Elder twin mortality	Dual mortality	Those with mortality	Those without mortality	p
Discordant twin (n:163)	30	3	14	47 (28.83%)	116 (71.17%)	<0.001
Concordant twin (n:473)	9	4	31	44 (9.30%)	429 (90.70%)	
Total (n:1172)	39	7	45	91 (7.76%)	545 (92.24%)	

blood diseases) were the first three issues. In twins with losses, only the existence of early membrane rupture (EMR) was statistically significantly high than other findings. While morbidity factors belonging to mother were higher in pregnancies where perinatal mortality was observed generally, statistically no significant difference was found (Table 8).

Discussion

Twin pregnancies recently have become as frequent as gestational diabetes or chronic hypertension in pregnancy. Therefore, when compared with singles, fetal and neonatal mortalities are 5-7 times higher in twin pregnancies. 25% of twins require intensive care service. In the long period, physical and mental problems are seen in this group more frequently. For example, cerebral palsy is found in twins 12 times higher and this rate only reduces to 3 times even delivery week is fixed.⁵ The main reason of this high perinatal morbidity and mortality are early deliveries and complications such as respiratory distress syndrome developed accordingly, necrotising enterocolitis and intraventricular bleeding.⁶ Thus, prematurity is responsible for _ of neonatal mortality and half of the long-term neurological complications.⁶ The increase in fetal malformations, intrauterine growth retardation, discordant growth, monochorionicity complications and intrapartum complications are the other reasons of morbidity mortality.⁷

Table 8. The relationship between maternal morbidity and perinatal mortality in twins.

	Twins without mortality (n: 545)	Twins with mortality (n:91)	P
Hypertensive diseases	44 (8.1%)	5 (5.5%)	>005
EMR	10 (1.8%)	7 (7.7%)	<0.01*
Systemic disease	10 (1.8%)	2 (2.2%)	>005
Other	5 (0.9%)	3 (3.3%)	>005
Total	69 (12.6%)	17 (18.7%)	>005

Developments in assisted reproductive techniques during last two decades in our country have been done thanks to technology, knowledge and experience and baby numbers going their home alive have increased. However, development in antenatal and neonatal care services could not keep pace with this speed.⁸ Though neonatal mortality reduces across the country, current developments indicate that problems especially in premature and severe premature cases will continue. In this study where we examined the outcomes of multiple pregnancies in some centers in Turkey, perinatal mortality rate was found as approximately 107 per thousand, rate of pregnant who lost any of fetuses during antenatal period or at delivery as 14% and rate of pregnant who lost all fetuses or newborns as 7%. According to clinical results reported in our country, in 1990s perinatal mortality rate of twins was found as 17% for those after week 28 in the retrospective study of Buyru et al.,⁹ 7.8% in the study of Karlık et al.,¹⁰ 7.8% in the study Kayıkçıoğlu et al.,¹¹ 8.9% in the study of Nas et al.¹² while it was

reported in 2000s as 7.7% in the study of Güney et al.¹³ where complicated cases were excluded from the series after week 24, 8.9% in the study of Yıldırım et al.¹⁴ where again some complicated cases were excluded. Kamacı et al.¹⁵ reported a high rate in Van which was 18%. The reason why our rate in our study was higher than other studies has been considered as including maternal complication cases and pregnancies over 20th week into the study.

Nassar et al.¹⁶ reported 26 perinatal mortality cases from 750 twin pairs (3.5%) in their study between 1984 and 2000 which included only one center and the smallest gestational week was excluded. In the present study, this rate three times higher. When both studies are compared, we consider that the most of the difference between two studies is caused by cases at too early weeks (20th-27th weeks) and non-existence of neonatal care department in half of our centers.

In our study, neonatal survival is at the lowest level in deliveries before 27th gestational weeks for twins. Mean delivery week (30th week) for mortality-observed twin pregnancies was approximately 2.5-8.2 weeks earlier than those where mortality was not observed (35th week). This rate was similarly given as 30th and 35th weeks in the study of Yıldırım et al.¹⁴

Dead fetuses died were the lighter ones in approximately $\frac{1}{2}$ of twins. While twin pairs born alive were 770g heavier than their dead pairs, it was 325g lesser than the birth weight mean of those who both born alive. This situation can be caused by the continuation of growth of living fetus after one is dead or by immediate born of fetus at normal limits after the loss of other fetus in the previous process.

It was claimed that one of the important factors affecting mortality in twins was the discordant

development among twins and it was reported that discordant twins had worse prognosis than concordant twins even there was no twin transfusion syndrome (TTS) or congenital anomaly.¹⁶ It was reported in the study of Nassar et al.¹⁶ that 12% discordant development (>25% weight difference) might be seen in those both born alive and that approximately 2/3 of mortality in discordant twins belonged to younger twin pair. When we evaluate same criteria in our study, we observed that discordance rate was similarly just below 16% and 90% of mortality belonged to younger twin pair. It was emphasized in another newborn study of 136 cases in our country that while mortality was not different, hypoglycemia and cesarean rates were found high in discordant twins.¹⁷ We consider that the difference in our study is caused by stillbirths which we excluded from our study.

Chorionicity is very important in terms of complications in twin pregnancies. For example, fetal risks are higher in monochorionic (MC) pregnancies than dichorionic (DC) pregnancies.^{14,18} While fetal loss rate is 1.8% in DC twins between 12th and 24th gestational weeks, it is 6 times higher in MC (12.2%). Perinatal loss risk after 24th gestational week is 1.6% in DCs while it is 2.8% in MCs. IUGR and preterm delivery risk is 2 times higher in MCs than DCs. Twin transfusion syndrome which is a serious complication for MC pregnancies affects approximately 15-20% of MC pregnancies and it is very important in terms of fetal morbidity and mortality.¹⁸ With death of one of monochorionic fetuses, there is a 38% chance that other surviving fetus may have mortality and 46% chance that it may have intracranial lesions.¹⁹ This rate explains us why cerebral palsy rate is high after death of a fetus in multi-

ple pregnancies with same genders. Also monoamniotic pregnancies proceed with 32% perinatal mortalities. Cord entanglement found in 71% of monoamniotic pregnancies has a leading role for this rate.¹⁹ In a wide twin series reported in our country, rate of dichorionics was 85% and in these dichorionics, perinatal mortality was 6%, monochorionics was 15% and perinatal mortality was 14%.¹⁴ Erdemoglu et al.²⁰ reported dichorionics as 69%, monochorionics as 31% while Üstün et al.²¹ reported dichorionics as 64% and monochorionics as 36%. It was not possible in our study to determine the chorionicity distribution due to both characteristics of questionnaire and deficiencies in general records.

Aslan et al.²² reported antenatal loss rate as 3.3% in their study where they examined single losses in their 972 cases of twin series and also stated that 31% of fetuses were lost after delivery. Zorlu et al.²³ found these rates as 3.8% and 12% respectively. Buyru et al.⁹ found death rate of single twin pair as 2.9%. Our single antenatal loss rate was 2.5% similarly. However, due to the characteristics of the study, time of antepartum mortality and its effect on other fetus could not be determined.

Mortality risk is higher in twins with same gender than those with different genders.¹⁹ Gender distribution in single losses was equal in our study. In dual losses, the dominance of losses from same genders (89%) was striking. This can be explained by the existence of monochorionic pregnancy. Besides, losses in girl-girl twins were almost two times more than boy-boy twins. Therefore, general loss rate in girls was also higher than boys. This finding can be explained by male fetuses being heavier than female fetuses and being born at a later gestational week (2243g versus 2089g).

According to the studies performed, 13-17% of twin pregnancies is delivered before 27th week or lighter than 1000g.^{9,10,15} Perinatal mortality is higher in them. A large number of twins are delivered in a period between 34th and 37th weeks called "late preterm period". Although mortality and morbidity are lower in this period compared to the period before 34th week, the low birth weight and risks of prematurity should not be overlooked.^{24,25} Moreover, it was shown that after 39th gestational week the perinatal mortality increases 13 times more than the period before.¹

In our study, while mortality was 100% in those born before 25th week or lighter than 500g, mortality reached to 5% as gestational weeks passed. The limit of relatively relative gestational week was determined as 30 while weight limit was determined as 1000g. No neonatal mortality was observed after 38th gestational week despite there was antenatal mortality.

Anomaly incidence in twins was reported between 3.6% and 6.3%.^{8-10,20,26,27} Gül et al.²⁶ reported 6.3% anomaly incidence in twins while they found 76% of them in a single fetus and they expressed that such type of discordant anomalies caused 22% increase in mortality (9% versus 31%). No comparison was performed in our series since anomaly and autopsy data were reported at a low rate.

When twins in our study are evaluated in terms of maternal morbidity, the existence of a significant relationship between EMR and fetus losses can only be explained by the occurrence of delivery after EMR and loss of preterm-premature fetuses. However, no statistical relationship was found in our study showing that systemic diseases were directly effective on losses.

Conclusion

One or more perinatal loss can be encountered in 15% of twin pregnancies today. In such cases, gestational week is earlier and birth weight is lighter. Gender uniformity, disproportionate growth, spontaneous multiple pregnancies (probably relatively increasing monochorionic pregnancies) appear as indicators intensifying mortality. Perinatal mortality only reduces after the limits of 30th gestational week and 1000g weight.

Though this multicentric study which is first in Turkey is narrow-scoped, it offers an insight into the twin deliveries between 2003 and 2004 and it may play a guiding role for studies to be performed later. To our knowledge, the most important way to decrease morbidity and mortality in multiple pregnancies is to keep early diagnosis records from the very beginning of pregnancy. Conservative approach for using assisted reproductive technique may also slow down the increase rate of multiple pregnancies. Using pregnancy certificate, providing communication between associations and physicians by computerized system, collecting data within a national database to be established and monitoring risky twins in perinatology centers will bring negative rates to an acceptable point.

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