Platelet count as a predictive factor of neonatal outcome in twin pregnancy with fetal demise

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Summary

Purpose: During the last decade, the rate of twin pregnancies has increased and reached 3% of all pregnancies. *Materials and Methods:* This study enrolled 36 twin pregnancies that were followed and delivered at the Clinic for Gynecology and Obstetrics, Clinical Center of Serbia over a five-year period. *Results:* The first group included 15 patients with a monochorionic twin pregnancy, and the second group consisted of 21 patients with a dichorionic twin pregnancy. The platelet count was significantly lower in patients with APGAR scores of more than 8, with an average of 185,000/ml, and in patients with a score of less than 4, the average count was 221,000/ml. The perinatal mortality rate of the surviving twin was 33% in the monochorionic group and 0.4% in the dichorionic group. *Conclusion:* An increase in the maternal platelet count can be used as a predictor for a negative neonatal outcome of the surviving twin.

Key words: Fetal demise; Twins; Platelet number.

Introduction

During the last decade, the rate of twin pregnancies has increased and reached 3% of all pregnancies. As mothers wait longer to have children and more of them use reproductive techniques, multiple pregnancies (mostly twins and triplets) have become more common. These pregnancies carry a higher risk for the mother and fetus, and obstetricians have developed more comprehensive regimens of check-ups and tests to minimize these risks [1]. The mortality and major morbidity rate that is associated with the death of one twin is reported to be 46%. When fetal demise occurs after midgestation, there is a 17% chance that the surviving twin in a monochorionic gestation will either die or suffer major morbidity. Morbidity and mortality approach 50% when twin-to twin transfusion is present. Major morbidity is unlikely to occur in the surviving twin of dichorionic gestations.

Major maternal problems are the result of coagulation disorders. Maternal coagulopathy following twin demise appears to be uncommon; however, coagulopathy has been reported to occur up to three weeks following fetal demise [2].

It is recommended that all twin pregnancies that result in a dead fetus be managed in tertiary referral centers with sufficient neonatal support. A management plan should be personalized to the patient. Intensive fetal surveillance is required and the determination of chorionicity, particularly in the first trimester, is crucial. Prompt delivery of the surviving twin following the death of a co-twin has not been shown to prevent the pre-existing neurological injury or other injury that occurred at the time of the death of the co-twin. Therefore, a delivery for the purpose of preventing injury should be weighed against the risks of premature delivery [3].

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Materials and Methods

The aim of this study was to analyze maternal coagulation status in twin pregnancies complicated by a single intrauterine death. Key maternal coagulation tests and their significance in predicting the neonatal outcome of the surviving twin were carefully studied.

This study enrolled 36 twin pregnancies that were followed and treated at the Clinic of Gynecology and Obstetrics, Clinical Center of Serbia, over a five-year period. The study was a retrospective (2004-2009) analysis, and it was approved by the Ethical Board of the Clinical Center of Serbia. Patients were divided into two groups that were similar in age, parity, method of conception, and termination of pregnancy. The first group included 15 patients with monochorionic twin pregnancies, and the second group consisted of 21 patients with dichorionic twin pregnancies. The antenatal records of the mothers, neonatal charts, and neonatal discharge summaries were reviewed. Autopsy and histology reports were also obtained. The approximate time interval between the death of the first twin and the delivery of the surviving co-twin was calculated from the information recorded in the case notes. Ultrasound scan data related to chorionicity, fetal growth, liquor volume, Doppler measurements, and a diagnosis of twin-to-twin transfusion syndrome (TTTS) were obtained.

The follow-up of the patients was conducted on a monthly basis at the clinic. Ultrasound follow-up included the biometry and Doppler flow measurements in the maternal and fetal circulation on an ACCUVIX ultrasound machine. Laboratory testing was performed in a biochemical laboratory on a Sysmex CA 1500 machine. The laboratory tests included prothrombin time (PT), partial thromboplastin time (PTT), platelet count, D-dimer, fibrinogen, and antithrombin (AT). After a pregnancy ended, an autopsy of the dead fetus and placenta was performed by an experienced clinical fetal pathologist.

The statistical analysis was performed using a chi-squared test, Student's t-test, Spearman's test, and Fisher's test (Statistical base, SPSS version 17).

Results

Multiple pregnancies are frequently the result of assisted reproduction procedures. In this study, multiple pregnancies represented 11 of all of the pregnancies. There was a significant difference between the two groups ($p = 0.35$). The majority of the monochorionic twins were conceived naturally (two in vitro fertilization (IVF) vs 13 natural), whereas dichorionic twins more frequently resulted from IVF (9 IVF vs 12 natural).

The average duration of pregnancy until fetal death was 4.8 ± 3 weeks in the first group and 6.3 ± 2 weeks in the second group. In all of the cases, the duration until fetal death was less than five weeks in 20, less than ten weeks in five, less than 15 weeks in five, and more than 16 weeks in six cases. There was no significant difference in the duration until fetal death between the groups (t = 0.326). Multiple significant correlations were observed between the duration of weeks until fetal death and the D-dimer levels, PT levels, week of delivery, and the birth weight of the dead twin. The D-dimer levels in the maternal blood increased with a longer duration until fetal demise ($p = 0.758$). The average D-dimer levels in the group of patients with less than five weeks until fetal demise occurred was 197 ± 8 µg/l, and in the group with more than 16 weeks, it was 214 ± 7 µg/l ($p = 0.375$). The average week of delivery was 33.1 ± 2 weeks in patients with less than five weeks until fetal death and 37.2 ± 1 weeks in patients with more than 16 weeks until fetal demise. Prolonged PT levels were present in three patients: one patient with less than five weeks until fetal demise, and two patients with more than 16 weeks until fetal death ($\chi^2 = 22$). No correlations were found between the duration of fetal demise and the levels of PTT ($\chi^2 = 6.5$), AT ($\chi^2 = 6.35$) and the platelet counts ($\chi^2 = 8$).

The laboratory tests performed to examine the maternal coagulation status were PT, PTT, platelet count, D-dimer, fibrinogen, and AT. The average PT value was 112 ± 7% in the first group and 108 ± 10% in the second group ($p = 0.617$). The average PTT was 28.76 ± 2 seconds in the first group and 29.8 ± 1.8 seconds in the second group ($p = 0.851$). The fibrinogen level was 4.59 ± 0.5 g/l in the first group and 5.2 ± 0.3 g/l in the second group. The D-dimer level was 257 ± 12 µg/l in the first group and 206 ± 5 µg/l in the second group . The AT level was 90 ± 2% in the first group and 89±1% in the second group ($p = 0.25$). The platelet counts were normal in all of the patients: 225,000 ± 1,500/l in the first group and 215,000 ± 2,000/l in the second group ($p = 0.47$). There was no significant difference between the study groups in any of the examined maternal coagulations parameters.

The analysis of the APGAR scores of the surviving twins indicated that three newborns died during Cesarean section delivery. These newborns were all monochorionic twins. One death was the result of a severe intrauterine infection and the other two deaths were the result of TTTS. There was a significant difference in the survivor mortality rates between the groups. In the monochorionic gestation group, the survivor mortality rate was 33%, and in the dichorionic gestation group, it was 0.4% ($p = 0.015$).

Severe perinatal asphyxia was detected in 11 newborns with APGAR scores of less than 4. Moderate perinatal asphyxia was detected in ten newborns with APGAR scores of less than 7. In total, only 12 babies were in good condition. There was no significant difference between the groups ($p = 0.08$). The degree of metabolic acidosis in the newborns correlated with the APGAR scores. A correlation was detected between the APGAR score and the time of delivery ($p = 0.568$), birth weight ($p = 0.566$), platelet count ($p = 0.501$), and duration until fetal death ($\chi^2 = 21.855$). The platelet count was significantly lower in patients with APGAR scores of more than 8, with an average of 185,000/ml, and in patients with a score of less than 4, the average count was 221,000/ml. No correlation was observed between other coagulation parameters and the APGAR scores of the newborns (D-dimer, $p = 0.4$; PTT, $p = 0.4$; and PT, $p = 0.35$).

Discussion

Krajenba *et al*. found an increased incidence of premature births in twin pregnancies with intrauterine fetal demise of one twin and an increased incidence of cesarean sections. He observed that the most frequent causes of death were monochorionicity and TTTS [4]. Sato *et al*. found an increased incidence of vascular thrombosis in the placentas of monochorionic twins with intrauterine growth restriction (IUGR) or intrauterine fetal demise [5]. Aslan *et al*. found that in a study of twin pregnancies with intrauterine fetal demise, 78% of the cases resulted in preterm delivery and 56% resulted in a Cesarean section, and the most common cause of death was TTTS [6]. In a study of twin pregnancies with a fetal anomaly in one of the twins, Chang et al. found that the incidence of fetal congenital anomaly was 2.4%; however, 56% of the healthy twins suffered an intrauterine death [7]. Malinowski *et al*. also analyzed the chorionicity of twins with the death of one fetus [8]. Johnson *et al*. observed that a favorable outcome of a pregnancy with the fetal death of one twin depends on the week of gestation when the death occurred and that twin pregnancies with different sexes have a better chance for survival [9]. Axt *et al*. showed that 71% of these pregnancies ended prematurely and had the same percentage of cesarean sections as in monofetal pregnancies, The expectative management of pregnancy was proposed [10]. Petersen *et al*. showed that the increasing incidence of prematurity in these pregnancies is more significant than the death of one fetus [11]. Vial *et al*. suggested that only a monochorionic twin pregnancy should be terminated as soon as possible, whereas in other cases, the pregnancy should be followed to term [12].

After delivery, the placenta should be examined macroscopically and histologically to determine placentation. Santema *et al*. have argued that other than chorionicity, histology is not informative because of the extensive secondary changes caused by the dead fetus. This low rate

of observation could be due to the collapse of the chorionic vessels of the dead fetus, which may make the recognition of the vascular communications difficult [13].

Conclusion

The antenatal and neonatal outcomes of twin pregnancies with the fetal demise of one twin are strongly dependent on the number of placentas. Monochorionic gestations are at an increased risk for fetal anomalies, TTTS, and the death of the surviving twin. Morbidity of the survivors was rare.

The incidence of maternal coagulation disorders was very low. Nevertheless, regular monitoring of the clotting system in maternal circulation is strongly recommended, and the authors suggest that D-dimer and PT testing are the most accurate methods for monitoring. An increase in the maternal platelet count can be used as a predictor for a negative neonatal outcome of the surviving twin. This can lead to consider aspirin or even anticoagulation therapy in these cases with platelet number more then 200,000 / ml. There is a place for further research in this area considering the increase of twin pregnancies.

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