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Original Research Article

Obstetric outcome in twin pregnancies complicated with single intrauterine fetal demise

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ABSTRACT

Background: It has been reported that single intrauterine fetal death in twin pregnancy occurs in 3.7-6.8% all twin pregnancies. The objective of this study was to evaluate the maternal and fetal demographic features and fetomaternal outcomes in twin pregnancies complicated with single intrauterine fetal demise and evaluation of available management guidelines.

Methods: This retrospective study was conducted at obstetrics and gynecology department of SGRRIM and HS, Dehradun, Uttarakhand between January 2015 and December 2019. There was a total of 182 twin deliveries at study hospital during this period and 35 of these cases were complicated with single intrauterine fetal demise. Maternal age, parity, chorionicity of twin gestation, gestational age at single intrauterine fetal demise, gestational age at delivery, mode of delivery, birth weight, Apgar Score at birth, neonatal intensive care unit stay of newborn, maternal fibrinogen levels during pregnancy and delivery time and associated obstetric complications were analyzed in these cases of single intrauterine fetal demise with twin gestation. All monochorionic twin pregnancies were included in the study Group A and dichorionic twin in Group B.

Results: The mean age of 32 patients included in study was 29.7±4.6 years. Twenty (62.5%) of these patients were dichorionic and 12 (37.5%) of these were monochorionic twin gestation. Single intrauterine fetal demise occurred in first trimester in 8 (25%) patients, during the second trimester 20 (62.5%) and 4 (12.5%) patients had third trimester single intrauterine fetal demise. Preterm deliveries occurred in 18 (56.3%) of patients and 8 (44.4%) of patients were of monochorionic and 10 (55.6%) of dichorionic twin patients. Among thirty-two patients, 11 (34.4%) patients had caesarean delivery and 21 (65.6%) patient had vaginal birth. No maternal or fetal mortality noted and none of the patients had maternal coagulation disorder.

Conclusions: This study indicates that in cases of twin pregnancies with single fetal intrauterine demise with individualized management plan at higher centre and close maternal and fetal surveillance live fetus can be saved without any maternal risk.

Keywords: Dichorionic, Monochorionic, Single fetal demise, Twin pregnancy

INTRODUCTION

It has been reported that single intrauterine fetal death in twin pregnancy occurs in 3.7-6.8% all twin pregnancies.^{1,2} Demise of one twin in the first trimester

does not affect the development of the surviving twin. The etiology is unknown in majority of cases and it could be either similar to that in singleton or unique to twinning process. The identifiable cause are twin-to-twin transfusion syndrome (TTTS), chromosomal and

congenital abnormalities, Rh incompatibility, placental insufficiency, intrauterine growth retardation related to preeclampsia, velamentous insertion of the cord, umbilical vein thrombosis, single umbilical artery and uterine malformations.^{3,4} Single intrauterine fetal demise may be associated with adverse outcomes in the surviving twin like prematurity, cerebral impairment and fetal death of second co-twin.⁵ Consequently, serial assessment of fetal growth and fetal well-being should be done.

In general, chorionicity (related to the placental angioarchitecture of inter-twin circulations), rather than zygosity, determines the risk of fetal morbidity and mortality. The perinatal mortality of monochorionic twin pregnancies is double in comparison to dichorionic twin pregnancies.⁶ The prevalence of monochorionicity in single intrauterine death in twins is 50% to 70%.^{7,8}

The most dreaded complication in single fetal demise is maternal coagulopathy which has been reported to occur in about 3-5 weeks following fetal demise. Therefore, an initial maternal coagulation profile with reassessment in 2-3 weeks or whenever clinically indicated is justified. Monitoring of maternal coagulation factor is not necessary when fetal loss occurs in first trimester.

Ideal management guidelines are still missing for twin pregnancies complicated with single fetal intrauterine demise. The frequency of maternal antenatal surveillance tests, ideal gestational age for delivery and associated short and long term fetomaternal sequel are still under debate. The purpose of this study was to explore the clinical features and fetal and maternal outcomes of twin pregnancies associated with the single fetal intrauterine fetal demise.

METHODS

This retrospective study was conducted in obstetrics and gynecology department of SGRRIM and HS, Dehradun, and Uttarakhand state during January 2015 to December 2019. Detailed demographic data includes age, parity, chorionicity, gestational age at fetal demise, gestational age at delivery, mode of delivery, maternal complication, maternal coagulation profile at time of first visit, follow up antenatal visits and at the time of delivery, birth weight, Apgar score at birth, NICU stay and any other short or long term fetal morbidity noted from all available records in obstetrics and pediatrics department.

Inclusion criteria

- During this time period, there were 182 twin deliveries. All patients with twin pregnancy complicated with single intrauterine fetal demise were included in the study. Thirty-two (17.6%) twin pregnancies complicated by single fetal intrauterine demise were included in the study. Of these 32 women 8 (25%) with twin gestation complicated by single fetal intrauterine demise after mid gestation

attended in study hospital as referred cases for the optimal management of mother and surviving co-twin

- According to chorionicity patients divided in Group A for monochorionic and Group B for dichorionic twin pregnancies and result were analyzed.

Exclusion criteria

- All women with single intrauterine fetal demise in multiple pregnancies other than twins were excluded from the study. During this study period, two cases were referred with the triplet IVF pregnancy with complication of single fetal demise.
- Cases with single intrauterine fetal demise in twin pregnancy with unavailable clinical details or who were lost to follow up before delivery were excluded from the study. A total of three such cases were excluded.

In this study, out of these 32 women, 24 (75%) have fetal demise in second and third trimester and 8 (25%) had single fetal demise in first trimester. These 32 women were managed till delivery with maternal and fetal monitoring protocols, as following:

Maternal monitoring

- All routine antenatal investigations were done (ABO Rh, Hb, OGCT/OGTT, urine routine and microscopy, viral markers)
- Coagulation profile (platelet count, PT, aPTT, BT and CT) at first visit and repeat coagulation profile at 2-3 weeks interval or whenever clinically indicated
- FDP and D-dimer when coagulation profile was deranged.

Fetal monitoring

- Determination of chorionicity and zygosity by available first trimester ultrasonography and correlated with the current ultrasonography
- Daily fetal movement count (DFMC)
- Biweekly USG with biophysical profile and color Doppler study
- Biweekly NST in pregnancies more than 32 weeks.

The diagnosis of twin-to-twin transfusion syndrome (TTTS) was based on the visualization of a separating membrane, polyhydramnios-oligohydramnios sequence in the absence of other causes of abnormal amniotic fluid volume, discordance in abdominal circumference or weight discrepancy greater than 20%. Non visualization of donor twin urinary bladder, abnormal fetal Doppler studies, hydrops or evidence of congestive heart failure were other findings suggestive of TTTS. All the pregnancies with gestational age less than 34 weeks were given steroids for fetal lung maturity. All cases were followed till onset of spontaneous labor if no obstetrical

indication for induction of labor identified. Caesarean delivery conducted only for obstetrical indications. After delivery, in few cases, placenta was sent for histopathology, dead fetus was examined for any gross anomaly and new-born was followed during neonatal period.

RESULTS

There were 182 twin deliveries at study hospital during the study period. Among these, 35 patients were diagnosed with complication of single intrauterine fetal demise. Three of these 35 patients were excluded from the study because of inadequate data. The remaining 32 twin pregnancies complicated by single intrauterine fetal demise were included in the study. The mean age of the

patients was 29.7±4.6 years. Thirteen (40.6%) of the patients were primigravida and 19 (59.4%) were multigravida. Twenty (62.5%) patients were dichorionic (Group B) and 12 (37.5%) were of monochorionic twin pregnancies (Group A) and chorionicity was confirmed with ultrasonography.

According to the gestational age at which single intrauterine fetal demise occurred, 8 (25%) patients had first trimester, 20 (62.5%) had second trimester and 4 (12.5%) patients had single fetal intrauterine demise in third trimester. Out of 32 patients, 18 (56.3%) patients had spontaneous twin conception, 2 (6.3%) conceived after ovulation induction, 3 (9.4%) conceived with intrauterine insemination and 9 (28.1%) had IVF twin conception.

Table 1: Maternal features of monochorionic (Group A) and dichorionic (Group B) twins.

Maternal features	Group A (n=12) Mean±SD	Group B (n=20) Mean±SD	p value
Maternal age (years)	30.9±5.6	28.5±3.6	>0.05
Gestational age at the time of single fetal demise (weeks)	19.4±7.4	23.6±6.5	>0.05
Gestational age at delivery (weeks)	34.6 ±2.4	35.4±3.6	>0.05
Maternal fibrinogen level at the time of fetal demise (mg/dl)	289±87.6	306±66.9	>0.05
Maternal fibrinogen level at the time of delivery	302±76.8	314±82.7	>0.05

Table 2: Fetal features of monochorionic (Group A) and dichorionic (Group B) twins.

Fetal features	Group A (n=12) Mean±SD	Group B (n=20) Mean±SD	p value
Gestational age at delivery (in weeks)	34.6 ±2.4	35.4±3.6	>0.05
Birth weight (grams)	1642±732	1876±564	>0.05
1-minute Apgar score	6.4±1.8	7.2±2.4	>0.05
5-minute Apgar score	8.9±1.1	8.2±1.8	>0.05
NICU stay (days)	26.2±5.4	20.3±6.4	>0.05

The mean gestational age at delivery was 34.6±2.4 weeks and 35.4±3.6 weeks in Group A and Group B respectively. The mean interval between fetal death and delivery was 68±27 days. The mean birth weight was 1642±432 gms and 1876±564 gms in Group A and B. The mean Apgar score for Group A, at one minute was 6.4±1.8 and the mean Apgar score at 5-minute of birth was 8.9±1.1 and Group B, mean Apgar score at one minute was 7.2±2.4 and the mean Apgar score at 5-minute of birth was 8.2±1.8. The mean maternal serum fibrinogen level at the time of delivery was 302±76.8 mg/dL and 314±82.7 mg/Dl in Group A and B respectively. The maternal and fetal features of Group A (monochorionic) and B (dichorionic) are shown in Table 1 and Table 2 respectively.

In Group A, 3 patients had preeclampsia, 3 had PPROM and 4 patients had IUGR and 2 patients had TTTS. In

group B, 3 patients had preeclampsia, 2 had preterm labor, and 3 had PPROM. In addition, one patient had antepartum hemorrhage due to placenta previa. Out of 32 neonates delivered 18 were admitted to NICU without any perinatal mortality and average duration of neonatal stay for Group A and B, were 26.2±5.4 and 20.3±6.4 days which were usually associated in preterm and IUGR neonates. Out of 32 patients included in this study, none of the patient had coagulation disorder. As shown in Table 1, no statistically significant ($p>0.05$) difference was found between the groups in terms of maternal fibrinogen levels at the time of first visit and delivery.

The frequency of preterm delivery was 66.7% among monochorionic twin pregnancies (Group A) and 57.4% among dichorionic twin pregnancies (Group B). The difference between the groups was not statistically significant ($p>0.05$).

DISCUSSION

The optimum management protocols for twin pregnancies complicated by single intrauterine demise are still missing. Many studies present insufficient data as to the management strategy to be followed in these cases. There are limited data in the literature which indicates the need of urgent deliveries following intrauterine demise.

According to the available literature, the first trimester single intrauterine fetal demise is not associated with any complications for the surviving co-twin.⁹ In this study, single intrauterine death in the first trimester occurred in 8 (25%) of the patients. The vanishing twin syndrome is a well-known phenomenon in twin pregnancies. The exact causes of embryonic loss, as well as the magnitude of the phenomenon are still not clear.

In monochorionic twins, the prognosis for the second twin is unknown and may be associated with neurological damage in the survivor co-twin.¹⁰ As signs of TTTS (discordant nuchal translucency) are not apparent before the second trimester, it is prudent to accept that embryonic loss during first trimester in monochorionic pregnancies is not associated with any increased morbidity in surviving co-twin. There are some literatures suggesting that loss of a twin in monochorionic pregnancies may lead to the twin reversed arterial perfusion sequence (TRAP). Follow up of the survivor with ultrasound and third trimester MRI to exclude brain and kidney abnormalities are suggested to confirm or refute the association.

Multicystic encephalomalacia and co-twin death in monochorionic pregnancies may occur due to the passage of thrombotic material from the dead to healthy twin following derangement in coagulation due to the death of one twin.¹¹ Another theory states that the haemodynamic imbalance theory which states that the placental anastomoses allow transfer of blood from the surviving twin to the dead co-twin giving rise to periods of hypoperfusion, hypotension and acute fetal anemia, resulting in neurological damage.¹² The detection of cerebral injury in the surviving co-twin during intrauterine period depends on the time interval from the insult to scan. Hemorrhagic lesions are visualized easily compared to ischemic injury. MRI has been shown to be helpful, and encephalography can detect antenatal necrosis of cerebral white matter.^{13,14}

Enbom has reported that the incidence of twin pregnancy with a single intrauterine death ranges from 3.5% to 7.8%.¹⁵ This study showed 17.6% incidence of single fetal death in twin pregnancies as compared to NCCP England (3.7%).¹⁶ The higher incidence might have been caused by the fact that in study hospital is a tertiary health care center that provides service for major Uttarakhand region. In a study conducted in Turkey, the incidence of this complication was reported to be 3.3%.¹⁷

In general, chorionicity rather than zygosity determines the risk of morbidity and mortality in twin pregnancies. Therefore, it is important to determine the type of placentation by ultrasonography. The perinatal mortality of monochorionic twin pregnancies is almost two times higher in comparison to dichorionic twin pregnancies.¹⁸ The cause of morbidity is mainly due to vascular anastomosis. Vascular anastomosis is more common in monochorionic placenta and can lead to TTTS, affecting the surviving co-twin, but this complication is rare in dichorionic placenta. In dichorionic twins, the prognosis for the surviving twins is relatively good and prematurity is the main risk factor. In monochorionic twins, the prognosis is poor and associated with neurological damage in the survivor.¹⁰

In this study, perinatal mortality was not observed in either group. This may be caused by the small number of cases in this study. The prevalence of monochorionicity in single intrauterine deaths in twins is 50% to 70%.⁷ Hilman et al, reported that the frequency of mortality in the surviving fetus was 15% in monochorionic twin pregnancies and 3% in dichorionic twin p number of patients in this study.¹⁸ Ong et al, reported this frequency as 12% in monochorionic twin pregnancies and 4% in dichorionic twin pregnancies.¹⁹ In this study, no intrauterine mortality documented in the surviving co-twin.

The association between the retention of the dead fetus in utero and maternal disseminated intravascular coagulation (DIC) was first notified by Weiner et al, and substantiated by Pritchard and Ratnoff for singleton pregnancies.^{20,21} They described the principal mechanism as a gradual reduction in the maternal fibrinogen level, according to the time interval from the intrauterine death to delivery. The DIC may progress in a slow and chronic manner. The fibrinogen levels return to normal in all cases within 48 hours of delivery. The exact underlying cause of the DIC is not established, there may be a breach between the maternal and fetal circulations, which allows the leakage of tissue thromboplastin from the dead fetus and its placenta into the maternal circulation. The transferred thromboplastin activates the extrinsic coagulation pathway, which consume platelets and coagulation factors. There is widespread intravascular coagulation and generation of fibrin. The presence of fibrin activates the fibrinolytic system, and plasminogen is converted to plasmin, which lyses fibrin into fibrin degradation products. The inhibition of fibrin polymerization may contribute to the defective haemostasis.²² Landy and Weingord have cited an incidence of maternal DIC of 25%.²³ There are few cases in the literature with maternal disseminated intravascular coagulopathy that occurred after the intrauterine death of one fetus in multiple pregnancies.^{24,25} In the present study, no patient had maternal coagulopathy. In addition, the difference between the two groups in fibrinogen levels at delivery and during pregnancy was not statistically significant.

The risk of preterm delivery before 34 weeks of gestation is increased in twin pregnancies complicated with single intrauterine fetal demise and is reported to be as high as 57%.²⁶ The risk of preterm is not affected by chorionicity.¹⁹ Pregnancy induced hypertension and pre-eclampsia has been found to be associated with the intrauterine death of one twin.^{1,7} This condition may be the cause of intrauterine death rather than the complication. Preterm birth is the common denominator of most adverse outcomes related to twinning in general and to monochorionic in particular. Kilby et al and Promper et al have suggested that the fetal outcome is mainly gestation- dependent and the goal should be to prolong pregnancy.^{1,26} The population based data suggest that as many as 30% of the stillbirths could have been avoided with elective preterm births at 34 weeks without any neonatal deaths among twins born at 34-35 weeks.²⁷ This observation supports that monochorionic twins may benefit from elective preterm birth but this issue is still very controversial. It has been suggested that after 37 weeks gestation, the surviving twin should be delivered once intrauterine death of the co-twin has been diagnosed.⁸ Evans et al advocated delivery at 32 weeks after documentation of lung maturity, even when the fetus is in no apparent distress.²⁸

At the study institute, follow up appointments were scheduled at every two weeks in all twin pregnancy complicated with single intrauterine fetal demise, fetal condition of surviving co-twin is evaluated by fetal Doppler studies, non-stress test (NST), and biophysical profile done at every two week or earlier when clinically indicated and further management depends on the current fetal condition. Maternal surveillance is done as in all twin gestations by monitoring of onset of PIH, gestational diabetes, preterm labor and specifically coagulation profile at first when patient reports with complication of single intrauterine fetal demise and repeated at two-week interval or when clinically indicated.

Important points in management protocols of single intrauterine fetal death in twin pregnancies are

- Counseling and support
- Individualized management protocols
- Management in a tertiary centre with well-equipped NICU
- Information and confirmation of chorionicity by imaging techniques
- Detailed evaluation of fetal anomalies and close fetal surveillance
- If preterm delivery is anticipated, Steroid prophylaxis for lung maturity
- Conservative management until 34 weeks
- Earlier intervention in presence of other obstetric or fetal indication
- Vaginal delivery whenever possible
- Post mortem examination of the stillborn and Placenta for histological examination if possible

- long term follow-up of survivor co-twin with pediatrician.

After delivery, the placenta should be examined grossly and histologically to determine the placentation but it is argued that other than chorionicity, histology is not informative as lots of secondary changes occurred in the vascular channels and tissue of placenta after the death of one fetus especially in monochorionic placenta.⁷ Post mortem examination of the dead fetus is also not very informative because of the long interval between fetal death and delivery during which tissue autolysis and maceration changes the finding of dead fetus.

In this study, caesarean delivery occurred in 11 (34.4%) and out of which 7 (63.6%) were monochorionic twin pregnancies. According to various studies, the rate of caesarean section varied considerably (19%-92%) and there is no specific contraindication to vaginal delivery, unless there is evidence of monoamniotic twins with a 25% increased risk of cord entanglement or knotting.^{8,11,29}

Parental anxiety and fear play an important role in the plan of management and often persuades the obstetrician to intervene. A multidisciplinary approach and effective counseling should be offered in such complicated cases.

One important aspect to be emphasized is psychological back-up for the survivor because surviving child may have guilty feelings towards the dead sibling, or the survivor may be blamed for the death of co-twin.

CONCLUSION

Twin pregnancies complicated with single fetal intrauterine demise must be followed up at higher center having good facilities of fetal and maternal monitoring and proper care with individualized management can minimize complications. The sequel of these patients depends on the chorionicity and gestational age. Intensive fetal surveillance is the key to salvage surviving co-twin.

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