

Fetal brain injury in survivors of twin pregnancies in single fetal intrauterine death – a short literature review

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ABSTRACT

Background. The incidence of multiple pregnancies is increasing in the last 10 years, along with the associated complications. Brain injuries and neurological complications associated with single fetal intrauterine death (sIUFD) are the most serious and have a negative impact on the surviving twin.

Methods. This review was performed by a single individual who searched via Google Scholar and Pubmed clinical studies which included sIUFD in monochorionic (MC) twin pregnancies. This research included studies from the last 10 years and the keywords used were: “single intrauterine fetal death”, “monochorionic”, “fetal brain lesions”, and “twin pregnancies”.

Results. After analyzing the clinical studies according to the keywords, only 15 studies (462 pregnancies) met the inclusion criteria. These included: monochorionic pregnancies and sIUFD that occurred after 14 weeks. The results of these trials showed a strong statistical association between single fetal intrauterine death and co-twin fetal brain lesions and neonatal death. Also, many of these recent studies mentioned the relationship between monochorionic city and preterm delivery, fetal growth restriction and twin–twin transfusion syndrome (TTTS).

Conclusion. Analyzing all these clinical studies, we can conclude that the intrauterine death of a twin in monochorionic pregnancies after the age of 14 weeks of gestation significantly affects the neurological development of the surviving twin.

Keywords: brain injury, a survivor of twin pregnancies in single fetal demise (sIUFD), twin pregnancies, vanishing twin syndrome (VTS)

INTRODUCTION

Along with the increase in assisted human reproduction procedures, the incidence of twin pregnancies also increased. They are more prone to major complications compared to single pregnancies. Perinatal mortality is considerably increased in multiple pregnancies, and intrauterine fetal death of one of the twins (sIUFD) represents a rare and serious perinatal complication [1]. Monochorionic pregnancies are more prone to fetal death in utero due to bidirectional placental vascular anastomoses.

The consequences of intrauterine fetal death are different depending on the gestational age at the time of the event, if it occurs after 14 weeks of gestation, it has been shown to have a more negative impact on the continuation of the pregnancy, and respectively the sur-

living twin. The co-twin has an increased risk of preterm birth, neurological complications, and death [2].

This article describes the types of brain lesions encountered in the surviving twin in the case of sIUFD as it causes an unfavorable long-term neurological outcome. In addition, we will detail the pathophysiological mechanisms and potential risk factors associated with the intrauterine death of a twin. Finally, we will present how to prevent brain injuries in co-twins and emphasize the lack of research in this field.

TYPES OF FETAL BRAIN INJURIES IN SURVIVOR TWIN

Brain lesions in the surviving twin were associated with intrauterine death after the 14th week of gestation.

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Van Klink et al. (2015) [3] described in their article that the most common brain lesions in newborns from twin pregnancies with a fetus that died in utero were: periventricular cystic leukomalacia, lesions in the basal ganglia, cortex, and thalamus, as well as vascular lesions in the area of the middle cerebral artery (MCA).

Prior to him, O'Donoghue et al., (2009) [4] showed that the death of one of the twins before 28 weeks can cause the surviving twin to develop lesions such as hemorrhage or multicystic encephalomalacia affecting the white matter, while after 28 weeks it also determines gray matter damage.

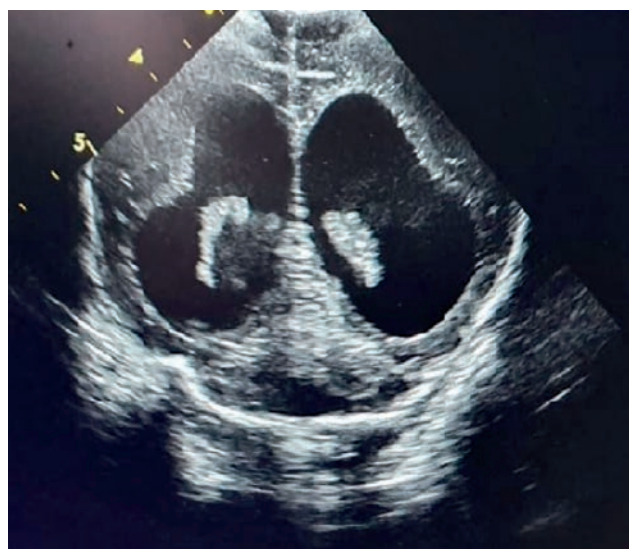


FIGURE 1. Periventricular cystic leukomalacia (personal collection – Dr. Andreea Avramescu Calomfirescu)

Also Mackie et al. (2019) [2] showed that the presence of abnormal antenatal brain imaging was reported in 20.0% (95% CI 12.8–31.1, I² = 21.9%, 6 studies, 116 pregnancies) of surviving monochorionic co-twins.

In 2022 Cruciat et al [1] classified the brain lesions in hypoxic-ischemic lesion of the white matter, hemorrhagic lesions, and vascular lesions.

PATHOPHYSIOLOGY OF BRAIN INJURY IN CO-TWIN SURVIVOR

Hillman et al. (2011) [5] reported that surviving twins after sIUFD from monochorionic pregnancies were more likely to have an abnormal cranial ultrasound postnatally versus dichorionic twins (34% [95%CI 28.8–46.1] vs. 16% [95%CI 7.8–23.5]). In the same study, he pointed out that twins from monochorionic pregnancies are more prone to develop an unfavorable neurological evolution, compared to dichorionic twins. (26% [95%CI 46.5–34.6] vs. 2% [95%CI 1.6–4.9]) due to a placental abnormality.

In 2016 Mackie et al. (2016) [6] concluded that the brain lesions in monochorionic pregnancies are

thought to be due to bidirectional inter-twin vascular anastomoses that form in MC placentation.

Another pathway that can cause brain injury in co-twin survivors after sIUFD was the thrombotic emboli theory, although this is disputed. Shek et al. in 2014 [7] concluded in their research that the theory is not favored.

Takita et al. (2019) [8], states that with the improvement of prenatal screening, the cases of intrauterine death caused by genetic anomalies decreased and those due to the umbilical cord and placenta anomalies increased.

In 2022 the pathophysiology of brain injury in co-twin survivors is still a widely debated issue.

RISK FACTORS FOR BRAIN INJURY

The factors most often incriminated in the occurrence of brain lesions in surviving twins are associated with: the gestational age at which the death of one of the twins occurs (van Klink et al., 2015) [3], monochorionic pregnancy (Hillman et al., 2011) [5] and the cause associated with a death such as TTTS (Griffiths et al. 2015) [9].

Morris et al. [10] published in 2020 one research about the incidence of the sIUFD and concluded that 27% sIUFDs were classified as spontaneous (i.e. no signs of TTTS, sIUGR or congenital/structural anomaly), 47% of pregnancies with a sIUFD were complicated by TTTS, 6% with sIUGR, and 15% with a congenital/structural anomaly and in 5% cases the cause was “unclear”.

Also, premature birth is another major risk factor. In 2013 Merhar et al. [11] published a study in which although the gestational age at birth did not correlate with the occurrence of brain lesions, it compared antenatal fetal brain MRIs with postnatal brain MRIs in twins with TTTS born prematurely and found a higher rate of brain injury postnatally of 68% (15/22) versus antenatally of 23% (5/22). Although the authors highlight they may not have had a sufficient number of cases to demonstrate statistical significance, due to an increase in the number of abnormal brain MRIs postnatally that would suggest that gestation age at birth does play an important role.

Odibo published in 2019 [12] a short review and mentioned the risk of preterm birth was increased almost five-fold in sIUFD but similar between monochorionic and dichorionic twins.

In a recent study published by Al-Alaiyan et al. (2022) [13] they found that delaying delivery in twin pregnancies complicated by single intrauterine demise with a good follow-up may lead to delivering infants with fewer complications of prematurity, also a fewer brain lesions.

PREVENTING BRAIN INJURY IN CO-TWIN SURVIVOR

Most of the research has focused on the early diagnosis of brain injuries and less on the ways of preventing them. In a 2016 study Mackie et al. [6] describe that the death of one of the girls in twin pregnancies occurs spontaneously without being able to be correlated with an underlying cause. Also, in pregnancies with complications, the incidence of brain injuries is lower due to screening.

Likewise, Simões et al. (2016) [14] state that careful follow-up of twin pregnancies and thorough prenatal screening decreases the rate of intrauterine fetal death in monochorionic twin pregnancies.

In a study published in 2022, with the improvement of prenatal screenings, Segev et al. [15] demonstrated that the presence of brain lesions identified with the help of fetal brain MR-imaging are lower in surviving twins (29 patients) vs those from normal pregnancies (49 patients) or from twin pregnancies without complications (28 patients).

DISCUSSION

Vanishing twin syndrome (VTS) and its relationship with brain lesions is a little-explored topic in obstetrics. For this reason, certain questions may arise. Are there other complications that persist long-term due to sIUFD? Do intrauterine brain injuries affect childhood development? The mystery behind the cases of brain damage in the surviving twin from VTS will persist until it will be better studied, on a larger number of twin pregnancies.

Parents bear a psychological burden in the case of sIUFD and this should not be underestimated. sIUFD

is a peculiar scenario, where mothers have conflicting feelings of joy that one child survived, but grief that the other died. The additional concern that the surviving twin may have long-term neurodevelopmental issues that may occur later in life is another factor to consider.

The surviving twin should be thoroughly examined and should enter a follow-up program for any neurodevelopmental issues. Head ultrasound and MRI examinations should be performed if there is any suspicion of brain damage.

By comparison with MRI, head ultrasound has lower sensitivity and specificity for the detection of non-hemorrhagic brain injury in newborns, although it is quickly and easily available.

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CONCLUSION

Monochorionic twin pregnancies are the most prone to intrauterine death of one twin, and this can cause significant brain lesions in the surviving twin. If the death occurs in the second or third trimester of pregnancy, the complications are greater and the survival rate is lower. Thus, the identification of early brain lesions during pregnancy can influence the decisions of future parents.

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