

# Twin-twin transfusion syndrome: what really matters concerning developmental outcome of survivals?

Síndrome da transfusão feto-fetal: o que realmente importa relacionado ao prognóstico do desenvolvimento nos sobreviventes?

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**T**win-twin transfusion syndrome (TTTS) is a condition unique to monochorionic pregnancies. Although not completely understood, the etiology relies on the presence of arterio-venous placental anastomosis that leads to an unequal blood exchange from one twin (donor) to the other (recipient). The presence of unbalanced placental vascular communications within a shared circulation is considered to be the main reason for its development. The net effect is a hemodynamic overload in one twin (recipient), and insufficiency in the other (donor), both situations carrying an increased risk for many organs and systems of the body.

TTTS is a serious condition that affects 10%-15% of twin pregnancies with monochorionic diamniotic placentation<sup>1</sup>. The natural history of untreated cases of TTTS carries a mortality rate of up to 90%, but the figures are largely dependent on the severity of the unbalance of the placental vascular anomaly. It accounts for 10%-17% of all perinatal mortality. Due to the increasing rates of twin gestations in recent years its incidence is increasing among all pregnancies<sup>2</sup>.

Numerous treatment options for TTTS have been used and, although the subject is still somewhat controversial, fetoscopic laser coagulation (FLC) is presently recommended to treat the condition<sup>3</sup>. A meta-analysis has shown that overall survival rates varies from 57% to 77% following FLC, and from 38% to 81% following serial amnioreduction, which is another method that is frequently used to treat TTTS<sup>4</sup>. FLC is used to convert a monochorionic placenta to a dichorionic one by occluding vascular connections between twins normally present in monochorionic placentas. Although these vascular connections are not the cause of TTTS, they are a necessary prerequisite for the syndrome development<sup>5</sup>.

Children born after a TTTS pregnancy are at increased risk of developmental abnormalities. There are several perinatal factors that are related to an increase in neurological morbidity, including premature birth and the neonatal disorders associated with pre-term birth, cardiac, renal and hematologic disorders.

Several studies have addressed the neurological outcome in TTTS survivors, the most recent ones being from children born to TTTS treated with FLC. The incidence of severe neurological abnormalities (cerebral palsy, mental retardation, blindness, deafness) ranged from 4% to 20%<sup>6,7,8,9,10</sup>. Van Klink et al. reported a decrease in severe neurological abnormalities when comparing two time periods, from 2000 to 2005, with 2008 to 2010, from 18% to 6%<sup>8</sup>.

The incidence of infants born prematurely in TTTS is high, and more than half of the babies are born with gestational age below 32 weeks<sup>8</sup>. Many gestational, neonatal and socio-economic variables were studied in relation to neurodevelopmental outcome in TTTS. Although it is difficult to compare the various studies, the most frequently reported were lower maternal education, higher Quintero stage (a stage frequently used to describe intensity of TTTS)<sup>6</sup>, and lower gestational age at birth<sup>6,8,9,10,11</sup>.

These findings point out the importance of pre-term birth and its associated neurological complications, including hypoxic ischemic encephalopathy, intracranial hemorrhage and

periventricular leukomalacia in the etiology of the brain lesions responsible for the adverse outcome seen in the affected children.

The spectrum of neurological abnormalities reported in children born after TTTS pregnancies is similar to that observed in low birthweight (LBW) babies follow-up<sup>12</sup>. With this in mind it is very important to follow these children up to a certain age in order to diagnose the most frequent neurological abnormalities observed in children born to TTTS pregnancies.

TTTS survivors are often born with LBW, most of them with very low birthweight<sup>13</sup>. Platt et al. studied 1,575 children with cerebral palsy that were born with very low birthweight ( $p \leq 1,500$  g). They found that 414 (26%) were of birthweight less than 1,000 g and 317 (20%) were from multiple pregnancies.

It is important to use the corrected age for prematurity when making developmental assessments up to one year of age. Otherwise, many healthy babies will be misestimated with developmental delay<sup>14</sup>. Most of the children that will

develop cerebral palsy at follow-up can be diagnosed around 12 months corrected age, and practically all of them at two years of age.

Abnormal language development, mental retardation, behavioral disorders, and learning disabilities are more often diagnosed after four to six years of age, sometimes even latter<sup>15</sup>.

TTTS treatment has been able to reduce significantly the death rate in fetuses. Modern neonatal care has decreased mortality and morbidity rates in LBW babies in the past decades. The main objective from now on is to try to reduce the prematurity rates observed in TTTS pregnancies, especially those with very low birthweight, which is the group at major risk for neurological sequelae.

The study of Arias et al. in this issue, is welcome because it reinforces the need of a detailed developmental follow-up of these children. We hope that the children included in their study group can be followed up to a later age to identify neurological abnormalities that cannot be diagnosed at an early age.

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