Twin Research and Human Genetics (2021), **24**, 37–41
doi:10.1017/thg.2021.7

CAMBRIDGE UNIVERSITY PRESS

Article

Perinatal Outcome of Selective Intrauterine Growth Restriction in Monochorionic Twins: Evaluation of a Retrospective Cohort in a Developing Country

Carolina Aquino[1,2], Ana Elisa Rodrigues Baião[1,2] and Paulo Roberto Nassar de Carvalho[1,2]

[1]Department of Obstetrics, Instituto Nacional de Saúde da Mulher, da Criança e do Adolescente Fernandes Figueira, Fundação Oswaldo Cruz (IFF/Fiocruz), Rio de Janeiro, Brazil and [2]Department of Obstetrics, Clínica Perinatal, Rio de Janeiro, Brazil

Abstract

Selective intrauterine growth restriction (sIUGR) in monochorionic twin pregnancies is associated with greater morbidity and mortality for both fetuses when compared to singleton and dichorionic pregnancies. This retrospective cohort study aimed to assess the perinatal outcomes of monochorionic twin pregnancies affected by this disorder and conducted expectantly, by analyzing the results according to the end-diastolic flow in the umbilical artery Doppler of the smaller twin (type I: persistently forward/type II: persistently absent or reversed/type III: intermittently absent or reversed). Seventy-five monochorionic diamniotic twin pregnancies with sIUGR were included in this study. sIUGR was defined by estimated fetal weight below the 3rd centile for gestational age, or below the 10th centile, when associated with at least one of the following three criteria: abdominal circumference below the 10th percentile, umbilical artery pulsatility index of the smaller twin above the 95th percentile, or estimated fetal weight discordance of 25% or more. Perinatal outcomes were analyzed from the prenatal period to hospital discharge and included perinatal death, neurological injury, retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), and sepsis. The mortality rate was 1.33% in this cohort. The overall morbidity rate was lower in type I twin pregnancies. In conclusion, this study shows that sIUGR type I has lower morbidity than types II and III in expectant management.

Keywords: twin pregnancy; monochorionic twins; selective intrauterine growth restriction; umbilical artery Doppler; neonatal morbidity; perinatal outcome

(Received 1 October 2020; accepted 27 January 2021; First Published online 22 March 2021)

Selective intrauterine growth restriction (sIUGR) occurs in 10 of monochorionic pregnancies and is associated with adverse perinatal outcomes, perinatal mortality, and neurological morbidity (Gratacos et al., 2012). The higher prevalence of prematurity in this population also increases the risk of retinopathy, bronchopulmonary dysplasia, necrotizing enterocolitis and sepsis (Flamant & Gascoin, 2013; Smits & Monden, 2011). A systematic review including 16 observational studies concluded that the risk of intrauterine death in sIUGR pregnancies conducted expectantly ranged from 3% to 16%, while the risk of perinatal morbidity was 9%–25%, according to the umbilical artery Doppler waveform (Townsend et al., 2019). The incidence of neurological injury is mainly associated with abnormal Doppler and low gestational age at birth (Inklaar et al., 2014).

The pathophysiology of sIUGR is explained by unequal placental territory sharing between fetuses and the pattern of placental anastomoses between fetal circulations (Gratacos et al., 2012). sIUGR has been classified into three clinical types with different evolution, according to the umbilical artery Doppler pattern of the smaller twin (Gratacos et al., 2007; Valsky et al., 2010). Type I sIUGR usually has a better prognosis, whereas types II and III are associated with poorer outcomes (Townsend & Khalil, 2016). In addition to expectant management, other options to be considered are umbilical cord occlusion and fetoscopic laser coagulation of vascular anastomoses (van den Bos et al., 2013). The application of fetal therapy is controversial and has been used mainly for sIUGR types II and III, before 24 weeks gestation (Bennasar et al., 2017; Valsky et al., 2010).

In 2018, a Delphi study was conducted to establish an international consensus in sIUGR definition (Khalil et al., 2019). While some experts used to consider the EFW <10th percentile for GA as an isolated criterion for the diagnosis of sIUGR, others included the EFW discordance or even the measurement of abdominal circumference (AC). Over the years, the lack of uniformity in the diagnostic criteria of sIUGR in previous studies has hampered the comparison of their findings and the determination of suitable parameters for follow-up and management of these pregnancies. In this study, we highlight this effort made by the scientific community and adopt Delphi consensus criteria to define sIUGR cases. The aim of this research was to evaluate

Author for correspondence: Carolina Aquino, Email: c.aquino1288@gmail.com

Cite this article: Aquino C, Rodrigues Baião AE, and de Carvalho PRN. (2021) Perinatal Outcome of Selective Intrauterine Growth Restriction in Monochorionic Twins: Evaluation of a Retrospective Cohort in a Developing Country. *Twin Research and Human Genetics* **24**: 37–41, https://doi.org/10.1017/thg.2021.7

mortality rates and perinatal outcomes in a retrospective cohort of monochorionic diamniotic (MCDA) pregnancies with sIUGR at two referral centers in a developing country.

Materials and Methods

This was a retrospective study, which included all MCDA twin pregnancies with sIUGR managed expectantly, delivered between 2010 and 2018 at IFF/Fiocruz and Clínica Perinatal, both referral centers in Maternal–Fetal Medicine in Rio de Janeiro, Brazil. Clinical data and outcomes were assessed exclusively by medical record review from the prenatal period to the newborns' hospital discharge. The study was approved by the local institutional ethics committee. Informed consent was applied, except for patients who were no longer followed by referral centers.

sIUGR was defined by Delphi consensus as estimated fetal weight (EFW) of one twin less than the 3rd centile or in the presence of at least two out of four contributory parameters: EFW less than the 10th percentile, AC of one twin less than the 10th centile, EFW discordance of 25% or more, and umbilical artery (UA) pulsatility index (PI) of the smaller twin above the 95th centile (Khalil et al., 2019). Intertwin EFW discordance was calculated using the following formula: (larger twin weight − smaller twin weight)/larger twin weight × 100% (Breathnach et al., 2011). All included cases were classified into three types according to the Doppler assessment of the umbilical artery, namely: type I, with end-diastolic flow persistently forward; type II, persistently absent or reversed (AREDF); type III, intermittently absent or reversed (iAREDF; Gratacos et al., 2007). The exclusion criteria were twin–twin transfusion syndrome (TTTS), except for spontaneous resolution of Quintero I, twin anemia–polycythemia sequence (TAPS), congenital anomalies, aneuploidies and genetic syndromes diagnosed during prenatal care or after birth. Dual IUGR cases and patients delivered in outside institutions were also excluded from the analysis. The diagnosis of TTTS and TAPS was based on an internationally accepted definition and polyhydramnios definition was not gestational age-dependent (Slaghekke et al., 2010; WAPM Consensus Group on Twin-to-Twin Transfusion et al., 2011).

During the 8-year study period, patients were referred by the public health system to the IFF/Fiocruz, where Doppler ultrasound was performed every 2 weeks from 16 weeks onwards for every MCDA pregnancy. At the perinatal clinic, patients underwent ultrasound follow-up when requested by their physicians in the supplementary health network, and close surveillance was suggested for sIUGR types II and III. sIUGR was clinically diagnosed by an EFW of <10th percentile in the smaller twin. The authors of this study had prospectively reviewed databases to include twins who fulfilled the requirements of the Delphi consensus (Khalil et al., 2019). The first and last ultrasound scans performed in referral centers were analyzed to classify pregnancies according to UA Doppler pattern and UA PI above 95th centile was defined by the Fetal Medicine Foundation reference ranges (Ciobanu et al., 2019). None of the sIUGR pregnancies in this study changed their initial classification prior to delivery. In both centers, decision making about delivery was conducted by prenatal caregivers. The screening of brain injuries was routinely performed by cranial ultrasound of neonates born premature or with suspected brain injury.

Primary outcome was defined as mortality from the intrauterine period to hospital discharge. Secondary outcomes were severe neonatal morbidity, defined by the presence of ultrasound finding of severe brain injury, retinopathy of prematurity (ROP) stage 3 or higher, bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) and/or sepsis. Cerebral injuries detected by cranial ultrasound of the neonates were divided into mild: intraventricular hemorrhages (classified according to Papile et al., 1978); grade I or II, periventricular leukomalacia (classified according to de Vries et al., 1992) grade I, subependymal pseudocysts and lenticulostriate vasculopathy; and severe, IVH grade III or IV and PVL grade II or III and porencephalic cysts. ROP was classified into five stages based on the International Classification of Retinopathy of Prematurity (International Committee for the Classification of Retinopathy of Prematurity, 2005).

BPD was defined for newborns until 31.6 gestational weeks as oxygen therapy >21% for at least 28 days after 36 weeks of postmenstrual age (PMA) or discharge to home, whichever comes first, or for those newborns from 32 weeks, oxygen therapy for more than 28 but less than 56 days postnatal age or discharge to home, whichever comes first (Jobe & Bancalari, 2001). NEC diagnosis was based on clinical signs and symptoms as well as radiological findings and, in some cases, surgically confirmed (Vermont Oxford Network, 2019). Sepsis was diagnosed and treated whenever clinically suspected, according to the International Pediatric Sepsis Consensus (Goldstein et al., 2005).

Statistical analysis was performed using SPSS software version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Analysis of variance (ANOVA) and Kruskal–Wallis test were used for comparisons between the three groups studied. Comparisons of continuous variables between groups were made using the Student *t* test or Mann–Whitney *U*-test. Chi-square test or Fisher's exact test were used, being appropriate to compare qualitative data. Logistic regression analysis was performed to evaluate the independent variables for morbidity and mortality. These were treated as combined outcomes, which included one or more of the following: ROP stage ≥ 3, BPD, NEC, sepsis, severe neurological injury and/or death. The results were presented as odds ratios and their respective 95% confidence intervals, and $p < .05$ was considered statistically significant.

Results

This cohort included 75 pregnancies, 67 (89.3%) classified as type I, 5 (6.7%) as type II, and 3 (4%) as type III, according to the UA Doppler pattern of the smaller twin. Twenty-nine pregnancies (38.6%) met criteria only based on EFW < 3%. There was no intrauterine fetal death in this sample.

Twin pregnancies affected by type I sIUGR had higher gestational age at diagnosis, less estimated fetal weight discordance, and greater birth weight. Those with type I also had a significantly later mean gestational age at birth (34.3 weeks), than those with type II (27.8 weeks) and III (28.3 weeks). Type II sIUGR had the lowest median birth weight in the smaller twin and the highest birth weight discordance, with a median of 43.3%. In type III, a lower median gestational age at diagnosis and a higher incidence of extreme premature births (<28 weeks) were found (Table 1).

We observed two cases (1.33%) of neonatal death until hospital discharge, one of them in the type III larger fetus and the other in the type I smaller fetus. Type I fetus was delivered at a gestational age of 29 weeks and 4 days due to hydrops with normal umbilical artery Doppler and no polyhydramnios. Sepsis was confirmed by positive blood culture for multidrug-resistant Gram-negative bacteria and the baby died after 14 days. A type III fetus was born at 27

https://doi.org/10.1017/thg.2021.7 Published online by Cambridge University Press

Table 1. Baseline characteristics of the study population according to the type of sIUGR

	Type I ($n = 67$)	Type II ($n = 5$)	Type III ($n = 3$)	p value
Maternal age (years)	31.6 ± 6.4	28.0 ± 7.4	40.3 ± 5.0	.033*
Multiparity (≥2 births)	9 (13.4)	0	1 (33.3)	.401**
Comorbidities				.299**
None	30 (44.8)	2 (40.0)	1 (33.3)	
Diabetes	2 (3.0)	0	0	
Hypertension	23 (34.3)	1 (20.0)	2 (66.7)	
Others	12 (17.9)	2 (40.0)	0	
GA at diagnosis (weeks)	29.7 (24.3–35.1)	24.8 (22.9–26.7)	24.3 (21–27.6)	.029*
EFW discordance (%)	17.8 (.9–53.1)	35.9 (18.9–54.0)	30.3 (24.4–31.5)	.009***
Birth weight larger twin (grams)	2267 (975–3210)	1170 (1020–1420)	1068 (910–1980)	.000***
Birth weight smaller twin (grams)	1872 (710–2675)	760 (560–830)	818 (590–1570)	.000***
Birth weight discordance (%)	13.4 (.0–43.9)	43.3 (18.6–51.3)	23.4 (20.7–35.2)	.004***
GA at delivery (weeks)	34.3 ± 2.4	27.8 ± .8	28.3 ± 2.3	.000*
< 28 weeks – n (%)	0	2 (40.0)	2 (66.7)	
≥28 to 31 weeks – n (%)	8 (11.9)	3 (60.0)	0	
≥32 to 36 weeks – n (%)	45 (67.2)	0	1 (33.3)	
≥37 weeks – n (%)	14 (20.9)	0	0	

Note: *Mean ± *SD*; **Proportions (%, *n*); ***Medians (range); GA, gestational age; EFW, estimated fetal weight.

Table 2. Mortality and morbidity of MCDA twin pregnancies according to the type of sIUGR

	Type I ($n = 134$)	Type II ($n = 10$)	Type III ($n = 6$)	p value
Neonatal death n (%)	1 (.7)	0	1 (16.7)	.004
Mild cerebral injury n (%)	11 (8.2)	3 (30.0)	2 (33.3)	.055
Severe cerebral injury n (%)	0	1 (10.0)	0	.942
ROP stage ≥3 n (%)	1 (.7)	0	1 (16.7)	.003
BPD n (%)	1 (.7)	3 (30.0)	2 (33.3)	.001
NEC n (%)	1 (.7)	1 (10.0)	2 (33.3)	.001
Sepsis n (%)	30 (22.4)	9 (90.0)	4 (66.7)	.001
Combined outcomes n (%)	30 (22.4)	9 (90.0)	4 (66.7)	.001
Length of stay (days) median (range)	12 (2–80)	70 (54–209)	40 (18–175)	.001

Note: ROP, retinopathy of prematurity; BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; combined outcome, severe brain injury and/or ROP stage ≥ 3 and/or BPD and/or NEC and/or sepsis.

gestational weeks and died after 20 days due to necrotizing enterocolitis. The overall incidence of cerebral injury was 10.7%, all detected by cranial ultrasound after birth. There was only one severe injury (IVH grade III), which occurred in a type II smaller fetus born at 27 weeks and 05 days, and 16 cases of mild cerebral lesions, divided into 12 IVH grade I, 3 IVH grade II, and 1 PVL grade I (Table 2).

One type I and one type III infant had ROP stage 3 (overall incidence, 1.3%). The incidence of NEC was 2.7% (4/150) in this cohort. BPD and sepsis were more frequent in types II and III ($p = .001$), with an overall incidence of 4% (6/150) and 28.6% (43/150) respectively. Combined outcomes, defined as the presence of any severe morbidity, was significantly higher ($p < .001$) in type II (*OR*, 9.0; 95% CI [.59, .98]) and type III (*OR*, 2.0; 95% CI [.30, .90]) compared to type I. Type II neonates had the longest hospital stay among the three groups (Table 2).

Multiple logistic regression analysis was carried out to measure the independent associations between clinical parameters (type II Doppler, isolated oligohydramnios, estimated fetal weight discordance of >35%, EFW <3rd percentile for gestational age, GA at diagnosis <22 weeks), and composite of neonatal morbidities and neonatal death (Table 3). After analysis, isolated oligohydramnios and GA <22 weeks at diagnosis were significant risk factors for poor outcomes.

Discussion

The classification of pregnancies affected by sIUGR according to the UA Doppler flow pattern of the smaller twin, proposed by Gratacos et al. (2007) is an important tool for prognostic guidance. However, the timing of delivery is crucial in perinatal outcomes, once a direct relationship between prematurity and morbidity

https://doi.org/10.1017/thg.2021.7 Published online by Cambridge University Press

Table 3. Multiple logistic regression analysis of morbidity and mortality predictors in sIUGR fetuses

	Nonadjusted *OR* [95% CI]	*p* value	Adjusted *OR* [95% CI]	*p* value
Type II	8.2 [.59, 115.5]	.117	–	–
Oligohydramnios	6.3 [1.2, 31.5]	.026	4.3 [1.1, 18.0]	.048
EFW discordance > 35%	.30 [.3, 3.5]	.301	–	–
EFW < P3 for GA	1.2 [.4, 4.5]	.446	–	–
GA < 22 weeks at diagnosis	6.3 [1.2, 32.1]	.014	5.7 [1.2, 27.8]	.028

Note: Outcome = brain injury and/or ROP stage ≥3 and/or BPD and/or NEC and/or sepsis and/or perinatal death.

and mortality is traditionally established (Khalil et al., 2019). Thus, similar studies can lead to conflicting perinatal results (Ishii et al., 2009; Weisz et al., 2011). This is the first study in the literature to use Delphi consensus criteria to present the correlation between UA Doppler and morbidity and mortality outcomes of MCDA pregnancies with sIUGR under expectant management, allowing a better comprehension of the studied population.

Brazil is a developing country of continental dimensions, with a population over 200 million people. Rio de Janeiro, where this study was carried out, is the third most populous city in the country. The absence of IUFD in our study might be due to the late inclusion of cases, since some of them were referred from the National Health System, in which first trimester ultrasound is not performed routinely and access to the referral service is difficult (Serra & Rodrigues, 2010). Therefore, we assume that our sample probably lost some fetal deaths in more severe cases that may have occurred before the patient could reach Maternal–Fetal Medicine services. Because of the small sample size, after birth mortality in this study were wide-ranging. Similar results were reported by other authors (Chang et al., 2010; Lopriore et al., 2012).

The low rate of neonatal death in this cohort is possibly associated with a higher incidence of type I sIUGR and consequently higher gestational age at birth. Despite the efforts of regulatory bodies, there is a wide variation between clinical guidelines recommendations and medical care, especially in the supplementary health system. Maternal–fetal specialists do not directly manage the timing of delivery. Although there is an international consensus for elective preterm delivery in pregnancies complicated by sIUGR, 19% of sIUGR type I patients had delivered after 37 gestational weeks in this study, one of them due to late inclusion of the patient in the public referral service and the others due to their own prenatal caregiver's decision.

Our study showed a statistically higher incidence of neurological injury in types II and III compared to type I sIUGR, as described by other authors who evaluated brain damage in these groups of fetuses (Chang et al., 2010; Inklaar et al., 2014). Although the present research did not propose to evaluate this finding more deeply, one of the current challenges is to establish the onset of neurological impairment of fetuses from sIUGR pregnancies. Researchers have suggested that neurological injury could not occur exclusively in the prenatal period, but soon after birth, related to the iatrogenic early delivery of these pregnancies (Buca et al., 2017).

Combined outcomes analysis showed a higher incidence of severe morbidities in type II sIUGR. The results of the present study support the hypothesis that MCDA twins affected by type I sIUGR have fewer perinatal morbidities when compared to types II and III (Ishii et al., 2009; Lewi et al., 2007; Towsend & Khalil, 2016). In contrast to a previous report by Cruz-Lemini et al. (2012), it was not possible to explore the association between extreme preterm birth and severe neonatal outcome due to its absence in type I twins. In our study, isolated oligohydramnios and diagnosis before 22 gestational weeks were found to be significant independent predictors for the occurrence of unfavorable outcomes in sIUGR twins. Despite the authors' choice to reclassify pregnancies through the Delphi consensus, perinatal outcomes were not affected, since all pregnancies included in this study met the anterior criteria of the smaller twin having an EFW of <10th percentile.

The natural history of sIUGR MC pregnancies has not yet been fully elucidated in the literature, and there is little evidence regarding the proper management of these pregnancies. There are important differences in mortality and neurological morbidity rates reported in different studies. This probably occurs not only due to the management outlined by individual characteristics but also due to the timing of delivery (Weisz et al., 2011). Our study was not designed to address intrauterine fetal therapy, such as cord occlusion or laser coagulation of placental anastomoses. Despite being a reasonable option before viability, fetal intervention was rarely performed in our hospitals for sIUGR, and those cases were excluded from our analysis. Brazil's legal barriers play an additional role in the option for noninvasive management, since termination of pregnancy is only allowed in cases of anencephaly, rape and risk of maternal death. Other cases with severe fetal impairment must undergo judicial authorization. Another partial impediment that has to be considered is the greater technical difficulty and higher complication rate of laser fetoscopy in sIUGR compared to TTTS (Bennasar et al., 2017).

The main methodological weaknesses of this study are its retrospective design and small sample size. Subanalysis of the sIUGR twins of types II and III might have been affected by the small number of included cases, precluding objective risk stratification of perinatal death and neurological injury. In conclusion, the study of sIUGR outcomes is challenging, mainly due to the lack of a standard definition before specialist consensus (Khalil et al., 2019). Most studies are also retrospective, nonrandomized and made with small samples. Despite the challenges in conducting scientific research in a developing country, which include late diagnosis, heterogeneity in clinical practice and legal barriers, our findings highlight lower morbidity related to type I fetuses and enhance the understanding of the perinatal morbidity of MCDA twin pregnancies with sIUGR, supporting the existing data. In terms of future research, further larger, randomized and prospective trials are warranted to determine neurological impairment and guide the optimal management of these pregnancies.

Acknowledgments. We would like to thank our participants for making this study possible.

Financial support. This research was supported by the authors.

Conflict of interest. None.

Ethical standards. The authors assert that this study was presented to the IFF/Fiocruz' Ethics Committee on Research and approved under the number 10103419.2.0000.5269, in accordance with National Health Council resolution 466/12.

References

Bennasar, M., Eixarch, E., Martinez, J. M., & Gratacós E. (2017). Selective intrauterine growth restriction in monochorionic diamniotic twin pregnancies. *Seminars in Fetal & Neonatal Medicine*, *22*, 376–382.

Breathnach, F. M., McAuliffe, F. M., Geary, M., Daly, S., Higgins, J. R., Dornan, J., Burke, G., Higgins, S., Dicker, P., Manning, F., Mahony, R., Malone, F. D., & Perinatal Ireland Research Consortium. (2011). Definition of intertwin birth weight discordance. *Obstetrics and Gynecology*, *118*, 94–103.

Buca, D., Pagani, G., Rizzo, G., Familiari, A., Flacco, M. E., Manzoli, L., Liberati, M., Fanfani, F., Scambia, G., & D'Antonio, F. (2017). Outcome of monochorionic twin pregnancy with selective intrauterine growth restriction according to umbilical artery Doppler flow pattern of smaller twin: Systematic review and meta-analysis. *Ultrasound in Obstetrics & Gynecology*, *50*, 559–568.

Chang, Y. L., Chang, S. D., Chao, A. S., Lien, R., Cheng, P. J., & Chueh, H. Y. (2010). Low rate of cerebral injury in monochorionic twins with selective intrauterine growth restriction. *Twin Research and Human Genetics*, *13*, 109–114.

Ciobanu, A., Wright, A., Syngelaki, A., Wright, D., Akolekar, R., & Nicolaides, K. H. (2019). Fetal Medicine Foundation reference ranges for umbilical artery and middle cerebral artery pulsatility index and cerebroplacental ratio. *Ultrasound in Obstetrics & Gynecology*, *53*, 465–472.

Cruz-Lemini, M., Crispi, F., Van Mieghem, T., Pedraza, D., Cruz-Martinez, R., Acosta-Rojas, R., Figueras, F., Parra-Cordero, M., Deprest, J., & Gratacós, E. (2012). Risk of perinatal death in early-onset intrauterine growth restriction according to gestational age and cardiovascular Doppler indices: A multicenter study. *Fetal Diagnosis and Therapy*, *32*, 116–122.

de Vries, L. S., Eken, P., & Dubowitz, L. M. (1992). The spectrum of leukomalacia using cranial ultrasound. *Behavioral Brain Research*, *49*, 1–6.

Flamant, C., & Gascoin, G. (2013). Devenir précoce et prise en charge néonatale du nouveau-né petit pour l'âge gestationnel. *Journal de Gynecolologie Obstétrique et Biologie de la Reproduction*, *42*, 985–995.

Gratacós, E., Lewi, L., Muñoz, B., Acosta-Rojas, R., Hernandez-Andrade, E., Martinez, J. M., Carreras, E., & Deprest, J. (2007). A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin. *Ultrasound in Obstetrics and Gynecology*, *30*, 28–34.

Gratacós, E., Ortiz, J., & Martinez, J. M. (2012). A systematic approach to the differential diagnosis and management of the complications of monochorionic twin pregnancies. *Fetal Diagnosis and Therapy*, *32*, 145–155.

Goldstein, B., Giroir, B., Randolph, A., & International Consensus Conference on Pediatric Sepsis. (2005). International Pediatric Sepsis Consensus Conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatric Critical Care Medicine*, *6*, 2–8.

Inklaar, M.J., van Klink, J. M. M., Stolk, T. T., van Zwet, E. W., Oepkes, D., & Lopriore, E. (2014). Cerebral injury in monochorionic twins with selective intrauterine growth restriction: A systematic review. *Prenatal Diagnosis*, *34*, 205–213.

International Committee for the Classification of Retinopathy of Prematurity. (2005). The International Classification of Retinopathy of Prematurity revised. *Archives of Ophthalmology*, *123*, 991–999.

Ishii, K., Osaka, I., Murakoshi, T., Takahashi, Y., Shinno, T., Matsushita, M., Naruse, H., Torii, Y., Sumie, M., & Nakata, M. (2019). Perinatal outcome of monochorionic twins with selective intrauterine growth restriction and different types of umbilical artery Doppler under expectant management. *Fetal Diagnosis and Therapy*, *26*, 157–161.

Jobe, A. H., & Bancalari, E. (2001). Bronchopulmonary dysplasia. NICHD/NHLBI/ORD Workshop Summary. *American Journal of Respiratory and Critical Care Medicine*, *163*, 1723–1729.

Khalil, A., Beune, I., Hecher, K., Wynia, K., Ganzevoort, W., Reed, K., Lewi, L., Oepkes, D., Gratacos, E., Thilaganathan, B., & Gordijn, S. J. (2019). Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: A Delphi procedure. *Ultrasound in Obstetrics and Gynecology*, *53*, 47–54.

Lewi, L. E., Mieke, M. C., Blickstein, I., Jani, J. C., Huber, A., Hecher, K., Dymarkowski, S., Gratacós, E., Lewi, P., & Deprest, J. (2007). Placental sharing, birthweight discordance, and vascular anastomoses in monochorionic diamniotic twin placentas. *American Journal of Obstetrics and Gynecology*, *197*, 587.e1–8.

Lopriore, E., Sluimers, C., Pasman, S. A., Middeldorp, J. M., Oepkes, D., & Walther, F. J. (2012). Neonatal morbidity in growth-discordant monochorionic twins: comparison between the larger and the smaller twin. *Twin Research and Human Genetics*, *15*, 541–546.

Papile, L. A., Burstein, J., Burstein, R., & Koffler, H. (1978). Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birth weights less than 1,500 gm. *Journal of Pediatrics*, *92*, 529–534.

Serra, C. G., & Rodrigues, P.H. A. (2010). Avaliação da referência e contrarreferência no programa saúde da família na região metropolitana do Rio de Janeiro (RJ, Brasil). *Ciência & Saúde Coletiva*, *15*, 3579–3586.

Slaghekke, F., Kist, W. J., Oepkes, D., Pasman, S. A., Middeldorp, J. M., Klumper, F. J., Walther, F. J., Vandenbussche, F. P. H. A., & Lopriore, E. (2010). Twin anemia-polycythemia sequence: Diagnostic criteria, classification, perinatal management and outcome. *Fetal Diagnosis and Therapy*, *27*, 181–190.

Smits, J., & Monden, C. (2011). Twinning across the developing world. *PLoS One*, *6*, e25239.

Townsend, R., & Khalil, A. (2016). Twin pregnancy complicated by selective growth restriction. *Current Opinion in Obstetrics and Gynecology*, *28*, 485–491.

Townsend, R., D'Antonio, F., Sileo, F. G., Kumbay, H., Thilaganathan, B., & Khalil, A. (2019). Perinatal outcome of monochorionic twin pregnancy complicated by selective fetal growth restriction according to management: Systematic review and meta-analysis. *Ultrasound in Obstetrics and Gynecology*, *53*, 36–46.

Valsky, D. V., Eixarcha, E., Martinez, J. M., Crispi, F., & Gratacós E. (2010). Selective intrauterine growth restriction in monochorionic twins: Pathophysiology, diagnostic approach and management dilemmas. *Seminars in Fetal & Neonatal Medicine*, *15*, 342–348.

van den Bos, E. M., van Klink, J. M. M., Middeldorp, J. M., Klumper, F. J., Oepkes, D., & Lopriore, E. (2013). Perinatal outcome after selective feticide in monochorionic twin pregnancies. *Ultrasound in Obstetrics and Gynecology*, *53*, 41–53.

Vermont Oxford Network (VON). (2019). *Vermond Oxford manual of operations part 2: Data definitions & infant data forms*. Retrieved from https://vtoxford.zendesk.com/hc/en-us/articles/360013115393-2019-Manual-of-Operations-Part-2-Release-23-2-PDF-

WAPM Consensus Group on Twin-to-Twin Transfusion; Baschat, A., Chmait, R. H., Deprest, J., Gratacós, E., Hecher, K., Kontopoulos, E., & Ville, Y. (2011). Twin-to-twin transfusion syndrome (TTTS). *Journal of Perinatal Medicine*, *39*, 107–112.

Weisz, B., Hogen, L., Yinon, Y., Gindes, L., Shrim, A., Simchen, M., Schiff, E., & Lipitz, S. (2011). Perinatal outcome of monochorionic twins with selective IUGR compared with uncomplicated monochorionic twins. *Twin Research & Human Genetics*, *14*, 457–462.