Original Article

Implementation of International Society Guidelines on Chorionicity Determination in Twins: A Multi-Center Cohort Study in Mainland China

Su-Wen Wu[1], Qiong-Jie Zhou[1,2], Xi-Rong Xiao[1], Yu Xiong[1], Huan Liang[1], Jie Shen[1], Jon Barrett[3], Hong Wang[1], Xiao-Tian Li[1,4]

[1]Department of Obstetrics, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China
[2]Women's Health and Perinatology Research Group, Department of Clinical Medicine, UiT - The Arctic University of Norway, Tromsø, Norway
[3]Sunnybrook Health Sciences Centre, Obstetrics and Gynecology, University of Toronto, Toronto, Canada
[4]Institute of Biomedical Sciences, Fudan University, Shanghai 200030, China

Su-Wen Wu and Qiong-Jie Zhou equally contributed to this article.

Abstract

Objective: Ultrasound determination of chorionicity is poor in early pregnancy in China. In an effort to increase the accuracy rate of prompt chorionicity determination, clinical training was provided to primary care physicians. This study assesses the effects of implementing clinical guidelines on chorionicity determination.

Methods: A multi-centered cohort study was conducted between January 2014 and June 2017 in 12 hospitals without fetal medicine centers. In 2014, the obstetricians and ultrasound physicians were trained in clinical practice and ultrasound examination relating to chorionicity determination. Linear and binary regression analyses were conducted to identify the effects of introducing the new protocols, including the diagnosis rate of chorionicty and perinatal outcomes, taking the data from 2014 as a baseline. Pregnancy outcomes were additionally adjusted for maternal age.

Results: During the period of this study, 3,599 twin pregnancies from 12 centers were enrolled, and a total of 2,998 twin pregnancies were extracted. The rate of overall chorionicity determination, including antenatal and postpartum diagnosis, increased successively from 49.5% in 2014 to 93.5% in 2017 ($P < 0.0001$). The rate of ultrasonic chorionicity diagnosis before 14 weeks increased from 25.2% in 2014 to 65.0% in 2017 ($P < 0.0001$). These changes were associated with decreasing incidence of preterm birth, a lower risk of stillbirth, whether for one ($P = 0.0456$ in 2016) or two fetuses ($P = 0.0470$ in 2016; $P = 0.0042$ in 2017) and a decreased rate of admission to neonatal intensive care unit (43.0% in 2014, 37.4% in 2017; $P = 0.0032$).

Conclusions: The implementation of a clinical practice guideline improved both overall and early chorionicity determinations. Regular training workshops of antenatal care are recommended to further promote capability in clinical diagnosis and treatment.

Key words: Chorionicity Determination; Clinical and Ultrasound Training; Community Hospitals; Guideline Implementation; Pregnancy Outcome

Introduction

With the development of *in vitro* fertilization and advanced maternal age, the incidence of twin births has risen dramatically over the past decades.[1-3] Twin pregnancies are at high risk of maternal and neonatal mortality and morbidity, especially sudden fetal death and intrauterine growth restriction (IUGR).[4-6] Compared with dichorionic gestations, monochorionic (MC) twins have an even higher

Access this article online

Quick Response Code:

Website: www.repdevmed.org

DOI: 10.4103/2096-2924.281857

Address for correspondence: Prof. Xiao-Tian Li, Department of Obstetrics, Obstetrics and Gynecology Hospital of Fudan University, No. 419 Fangxie Road, Shanghai 200011, China
E-Mail: xiaotianli555@163.com
Dr. Hong Wang, Department of Obstetrics, Obstetrics and Gynecology Hospital of Fudan University, No. 419 Fangxie Road, Shanghai 200011, China
E-Mail: doctorwanghong@126.com

Submitted: 02-Dec-2019 **Revised:** 31-Jan-2020 **Accepted:** 26-Feb-2020
Published: 02-Apr-2020 **Edited by:** Yong-Qing Zhu.
How to cite this article: Wu SW, Zhou QJ, Xiao XR, Xiong Y, Liang H, Shen J, Barrett J, Wang H, Li XT. Implementation of International Society Guidelines on Chorionicity Determination in Twins: A Multi-Center Cohort Study in Mainland China. Reprod Dev Med 2020;4:42-52.

risk for adverse pregnancy outcomes due to shared placental circulation, which may lead to its own complications, for example, twin-to-twin transfusion syndrome (TTTS), twin anemia polycythemia sequence, twin reversed arterial perfusion, and selective fetal growth restriction.[4,7-9] Moreover, preterm delivery and intrauterine death are also more frequent in MC twins.[4,9-11] Therefore, early and accurate ultrasound determination of amnionicity and chorionicity is beneficial for further appropriate antenatal management and surveillance.

The accuracy was nearly 100% for the determination of chorionicity by ultrasound performed at 11–14 weeks; in contrast, the error rate was up to 10% when chorionicity was diagnosed after 14 weeks.[12-14] Thus, chorionicity should be determined at the first ultrasound, preferably in the first trimester. Guidelines on twin pregnancy from the Society of Obstetricians and Gynecologists of Canada, the National Institute for Health and Clinical Excellence, the International Society of Ultrasound in Obstetrics and Gynecology, and the French College of Gynecologists and Obstetricians all recommended that the first-trimester ultrasound should be performed for the diagnosis of pregnancy and chorionicity determination.[15-18] Chorionicity determination was also recommended by guidelines published by the China Medical Association in 2015. Chorionicity can be determined using the number of gestational sacs, amniotic sacs within the chorionic cavity, and yolk sacs before 10 weeks gestation. Between 10 and 14 weeks, sonographic findings, such as a chorionic peak or the placental number, will help diagnose amnionicity and chorionicity.[15] However, guidelines are not always translated into policy or practice.[19,20] Despite all the evidence that ultrasound should be generalized in the identification and management of twin pregnancies, challenges still exist in implementing the guidelines for twin pregnancy management.[13,21]

There was a problem in China with the determination of chorionicity by ultrasound in the first trimester of pregnancy, which was due to community hospitals lacking in early ultrasound expertise. We set out to increase the rate of prompt chorionicity determination through training primary care physicians. In 2014, obstetricians and ultrasound physicians in 12 community hospitals were trained in the clinical practice and ultrasound examination of chorionicity determination by professional clinicians from tertiary medical centers. Women pregnant with twins, who had high-risk factors, would be transferred to the tertiary medical centers. The chorionicity determination rate in each center was investigated annually to improve the quality of clinical training sustainably. We implemented the clinical practice guidelines on chorionicity determination in 12 centers during the period between 2014 and 2017. For our article, the overall and early diagnostic rate of chorionicity and relative pregnancy outcomes would be evaluated to reveal the effects of this management strategy. We presented evidence of a shortage of chorionicity determination in community hospitals and developed approaches to improving the management of twin pregnancies in these hospitals.

Methods

Study design and setting

This multi-centered study was conducted through the implementation of existing guidelines on the determination of chorionicity by ultrasound in the first trimester, with the primary aim of evaluating temporal trends after clinical training in twin pregnancy and preliminary screening for complications. The Hospital Committee for Medical Research Ethics of Obstetrics and Gynecology at the Hospital of Fudan University approved the study (2017–44). This study was conducted in 12 community hospitals in China from January 2014 to June 2017. These were the Cixi Women and Children's Hospital, the Haiyan Women and Children's Hospital, the Jiading Women and Children's Hospital, the Lianyungang Women and Children's Hospital, the Nantong Women and Children's Hospital, the Fourth People's Hospital of Ningbo, the Taian Women and Children's Hospital, the Yangzhou Women and Children's Hospital, the Zhuzhou Women and Children's Hospital, the Xuzhou Women and Children's Hospital, the Kunshan Women and Children's Hospital, and the First People's Hospital of Kunshan.

Participants

The sample size was estimated by the number of women pregnant with twins who had their first visit to our research units during the study period. Those eligible for our sample were women between the ages of 18 and 50 with a twin pregnancy who took regular antenatal examinations in our centers. Twin pregnancy was diagnosed by the first ultrasound. Exclusion criteria included where there were key data missing, importantly, chorionicity and delivery outcomes, especially twin pregnancies with the death of one or two fetuses before delivery and miscarriage. A "twinning investigation handbook" was used to record demographic information, diagnosis of chorionicity, and perinatal outcomes. Pregnancy outcomes were followed up whether patients had early chorionicity determination or not.

Implementation of chorionicity determination guidelines

Professional training

In 2014, obstetricians and ultrasound physicians in community hospitals were provided with clinical practice and ultrasound examination training by professional clinicians from tertiary medical centers as follows: (1) ultrasound physicians attended a 2-day ultrasound training in twinning pregnancy, including the early diagnosis of chorionicity by ultrasound. Routine quality control was made every 3 months thereafter by spot check of saved ultrasound images. (2) Obstetricians attended a 2-day clinical training, including the treatment and follow-up during twinning pregnancy and the detection of women with high-risk factors requiring transferal to the tertiary medical centers.

In this project, there were two or more specialized obstetricians and one or two ultrasound physicians sequestered to deploy this twin pregnancy management strategy in each community hospital. Furthermore, each hospital was assigned a

corresponding tertiary medical center to receive some high-risk patients who may be transferred.

Process of medical care

Once diagnosed with a twin pregnancy in the first trimester, women were scheduled to have a "twinning ultrasound" examination before the gestational age (GA) of 14 weeks, and their ongoing obstetric visits were scheduled according to the clinical practice guidelines. Those women with dizygotic twinning had ultrasound detection every 4 weeks, whereas those with monozygotic twinning were examined every 2 weeks, together with a middle cerebral artery (MCA) examination. If, however, the patients had a first-time consultancy after 14 weeks, the chorionicity determination would be performed by placental examination at delivery.

Women with the following risks were recommended for transferal to the tertiary medical centers: (1) possible fetal growth discordance: Δ crown-rump length ≥20% or Δ abdominal circumference ≥20% or Δ estimated fetal weight (EFW) ≥20%, (2) abnormal umbilical flow index or abnormal MCA, (3) abnormal amniotic fluid index, (4) possible fetal abnormality, and (5) other risks including fetal edema and maternal complications needing further treatment.

Outcome evaluation

The primary outcomes included the overall, early, and postpartum chorionicity determination rates during the study period of 2014–2017. Chorionicity was determined using the following points: (1) if GA was before 10 weeks, the number of embryo sacs, the number of amnion sacs, and the number of yolk sacs were detected by ultrasound; (2) if GA was after 10 weeks, the number of placentae, any twin peak, the thickness of the fetal membrane, and whether the placenta was separated were detected by ultrasound.

The secondary outcomes were pregnancy outcomes included basic delivery information, common perinatal complications, and specific twin pregnancy complications. Basic delivery information included parity, GA at delivery, and neonatal birth-weight. GA was diagnosed based on the date of the last menstrual period and further confirmed by an early prenatal ultrasonogram if available. GA at delivery can be helpful to distinguish the iatrogenic preterm labor between dichorionic and MC twins. Perinatal complications referred to pregnancy-related diseases – the presence of either neonatal death, stillbirth, admission to neonatal intensive care unit (NICU), or an Apgar score of less than seven. Hypertensive disorders of pregnancy included gestational hypertension; preeclampsia; eclampsia; and "hemolysis, elevated liver enzymes, and low platelets" syndrome.[22] A 75 g oral glucose tolerance test for gestational diabetes mellitus (GDM) was performed.[23] Neonatal death was death during the first 0–27 days after live birth. Specific twin pregnancy complications of MC gestations were assessed by ultrasound, including TTTSs, and selective IUGR (sIUGR).[15,24,25] sIUGR was diagnosed if the difference of EFW at the last ultrasonic examination before delivery was more than 20%.[26]

Statistical analysis

A total of 12 community hospitals containing 3,599 twin pregnancies participated in this project [Figure 1]. We eventually excluded the Xuzhou and Kunshan Women and Children's Hospitals from the analysis because of incomplete data from the survey years (9.9%, 356/3,599). The First People's Hospital of Kunshan participated only after 2016, and their annual data were not comparable with the other hospitals (6.8%, 245/3,599). All twinning pregnancies in the other nine centers have been enrolled for the final analysis.

In our analysis of the primary outcomes, we included all twin pregnancies from the nine centers (83.8%, 2,998/3,599) to compare the changes in overall and early chorionicity determination rates and maternal and neonatal outcomes. We further analyzed the rate of different kinds of twins to verify the reliability of the data from these nine centers. Due to the small total number of pregnant women in the Cixi Women and Children's Hospital ($n = 4$ in 2014), the Haiyan Women and Children's Hospital ($n = 12$ in 2014, $n = 8$ in 2015, $n = 9$ in 2016, and $n = 8$ in 2017), as well as the Fourth People's Hospital of Ningbo ($n = 4$ in 2014), the constituent ratio was relatively volatile.

For a subgroup analysis of chorionicity, we divided twin pregnancies into three subgroups: MC diamniotic (MCDA), MC monoamniotic (MCMA), and dichorionic diamniotic (DCDA). We deleted patients with missing chorionicity determination (0.6%, 23/3,599), patients whose chorionicity was undiagnosed (19.7%, 710/3,599), or the diagnosis time was ambiguous (9.9%, 357/3,599). More specifically, patients with ambiguous chorionicity diagnosis time were those who had chorionicity determination after the GA of 14 weeks but still prenatally. In order to compare the neonatal outcomes, we further excluded patients who did not deliver at these facilities during the study period (0.4%, 16/3,599). This method resulted in a total of 1,892 patients included in the analysis.

Statistical analysis was performed using IBM SPSS version 21 (SPSS Inc., Chicago, IL, USA). We conducted linear regression and binary regression analyses. The data in 2014 were taken as the baseline. We considered maternal age and parity as potential confounders, and we finally included maternal age into the regression analysis due to its significant difference between survey years and correlation with fetal and infant death.[27,28] We conducted a sensitivity analysis with the exclusion of those with no data for maternal age. For an analysis of the risk factors of neonatal outcomes, we carried out another sensitivity analysis, adjusting for pregnancy-related diseases. $P < 0.05$ was considered statistically significant.

Results

General parameters

During the period 2014–2017, 3,599 twin pregnancies from 12 centers were enrolled, and a total of 2,998 twin pregnancies were extracted. We analyzed the annual incidence of different

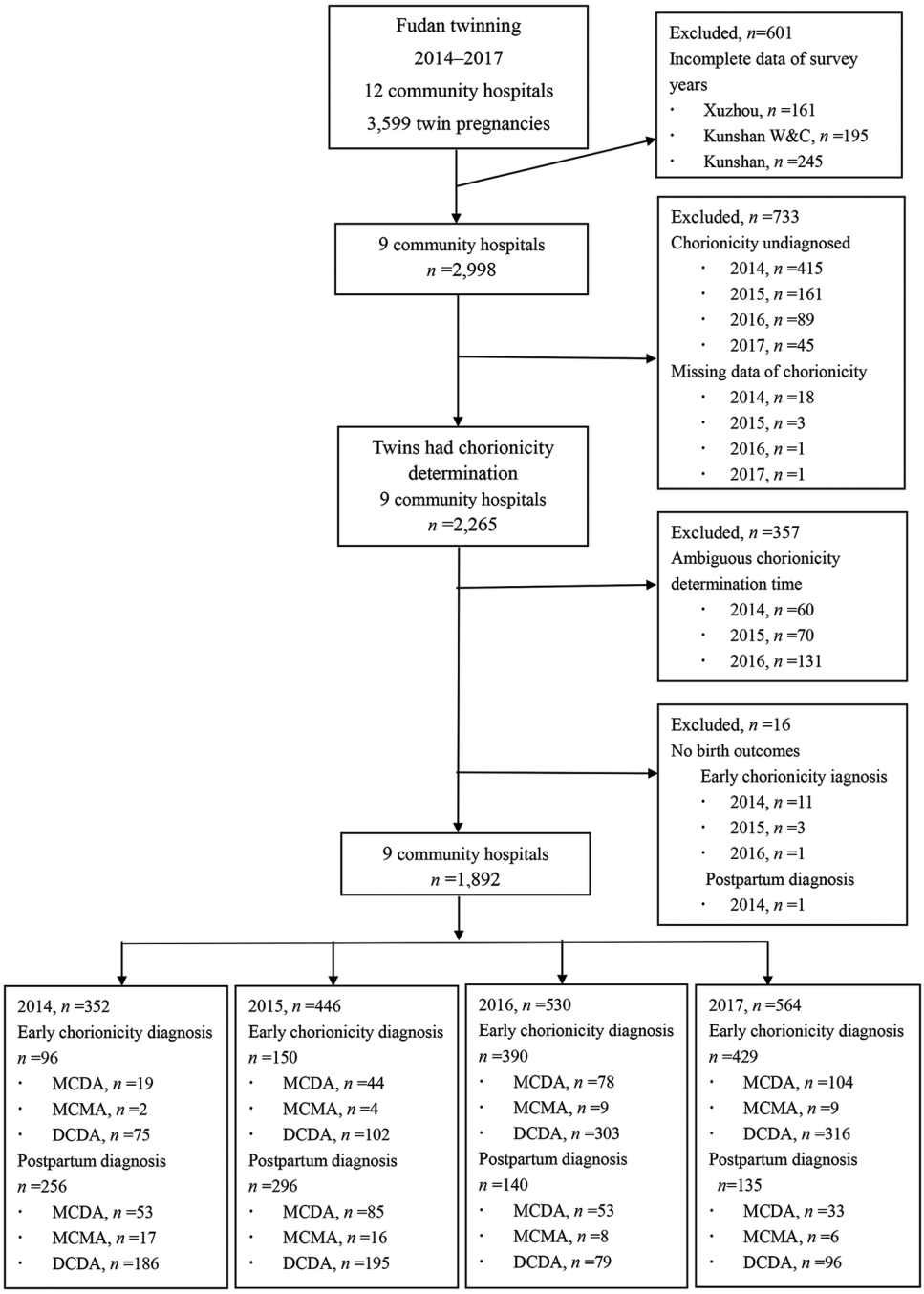

Figure 1: Flow chart of participants.

twin types in each center as part of our quality control. The twin constituent ratio was roughly stable [Figure 2]. The annual incidence of MCDA was 21.7% in 2014, 30.3% in 2015, 27.2% in 2016, and 25.6% in 2017. The incidence of MCMA was 5.9% in 2014, 4.6% in 2015, 3.5% in 2016, and 2.9% in 2017. The incidence of DCDA was 72.4% in 2014, 65.1% in 2015, 69.3% in 2016, and 71.5% in 2017.

The main characteristics of the study population are presented in Table 1. There was no significant difference in the percentage of nulliparous women, whereas the average maternal age increased annually and was significantly higher in 2017 ($P < 0.0001$). We finally included maternal age in the regression analysis because of its significant difference between the survey years and correlation with fetal and infant death.[27,28]

Chorionicity determination rate increased after training

The annual data on the chorionicity determination rate in each center are shown in Figure 3. Compared with the chorionicity determination rate in 2014, 49.5% of 857 twin pregnancies, the rate raised successively to 76.0% in 2015 ($P < 0.0001$), 88.0% in 2016 ($P < 0.0001$), and 93.5% in 2017 ($P < 0.0001$). Among patients who received a chorionicity determination,

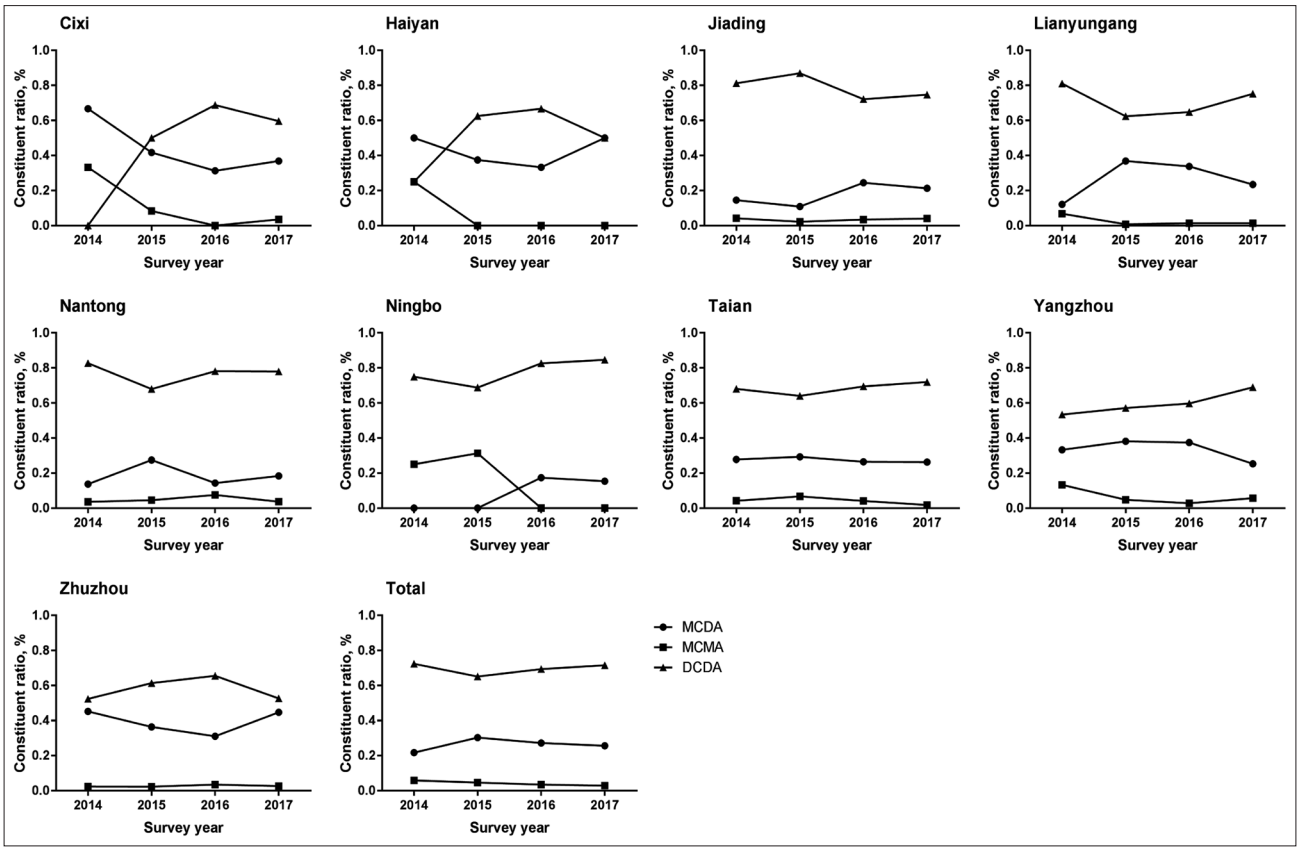

Figure 2: The constituent ratio of monochorionic diamniotic; monochorionic monoamniotic; and dichorionic diamniotic in each center. In the Cixi Women and Children's Hospital (n = 4 in 2014), the Haiyan Women and Children's Hospital (n = 12 in 2014, n = 8 in 2015, n = 9 in 2016 and n = 8 in 2017), as well as the Forth People's Hospital of Ningbo (n = 4 in 2014), the number of pregnant women is lower than that in the other six centers.

the number of patients undergoing ultrasound diagnosis before GA of 14 weeks increased significantly during the survey years. The early chorionicity diagnostic rate increased to 29.5% in 2015 (P = 0.1453), 59.1% in 2016 (P < 0.0001), and 65.0% in 2017 (P < 0.0001), when compared with that in 2014 (25.2% of 424). Meanwhile, postpartum chorionicity determination rates declined year by year after clinical training (P < 0.0001) [Table 1]. Among the nine centers, the Lianyungang and Nantong Women and Children's Hospitals demonstrated the least improvement after training.

Pregnancy outcomes before and after training

After correction of maternal age, the incidence of hypertensive disorders of pregnancy and GDM showed no statistical differences from 2014 to 2017, whereas the prevalence of other pregnancy-related diseases showed significant differences (2015, P = 0.0366; 2016, P = 0.0011; 2017, P < 0.0001) including anemia, abnormal thyroid function, liver function damage, thrombocytopenia, intrahepatic cholestasis of pregnancy, placenta previa, and other diseases. Prompt chorionicity determination was associated with a lower risk of extreme preterm delivery, from 4.2% in 2014 to 1.0% in 2017. The rate of GA of delivery between 32 and 34 weeks also declined, from 8.8% in 2014 to 5.8% in 2017. The incidence of stillbirth, including one or two fetuses, was decreased, together with increased birth weight and decreased risk of admission to the NICU. The results suggest that prompt chorionicity determination, if followed up in medical diagnosis and treatment, can improve the outcomes of twin pregnancy. No significant difference was seen in Apgar scores of less than seven, TTTS, FGR, and sIUGR [Table 1].

Effects of early chorionicity determination on different types of twins

In order to explore whether an elevated chorionicity determination rate has an influence on the specific outcomes of MCDA, MCMA, and DCDA pregnancies, we further filtered the data, and 1,892 cases were extracted. The results were based on those pregnant women with accurate chorionicity diagnosis time and birth outcomes. We deleted neonatal death from the annual comparison of pregnancy outcomes because there was only one case in the final cohort. When classified by twin subtypes, it seemed that early chorionicity determination tended toward a lower severe neonatal mortality risk in MCDA pregnancies. We found that the stillbirth rate of MCDA decreased after 2014 (0.8% in 2015; 2.3% in 2016; 1.5% in 2017) without statistical difference (2015, odds ratio [OR] = 0.18, 95% confidence interval [CI] = 0.02–1.78; 2016, OR = 0.57, 95% CI = 0.11–2.90; 2017, OR = 0.37, 95% CI = 0.06–2.29). Similarly, there was no significant

Table 1: The demographic information, chorionicity determination, and pregnancy outcomes of twin pregnancies from 2014 to 2017

	2014 *n* = 857	*P*	2015 *n* = 683	*P*	
				Crude model	Adjusted model*
Maternal age (years)	28.02 ± 4.61	Ref	28.30 ± 4.61	0.2388	0.2388
<20	2.3% (19/826)		2.4% (16/660)		
20–34	88.0% (727/826)		86.1% (568/660)		
≥35	9.7% (80/826)	Ref	11.5% (76/660)	0.2236	0.2236
Parity					
Primiparous	63.4% (542/855)		60.3% (410/680)		
Multiparous	36.6% (313/855)		39.7% (270/680)		
Pregnancy-related diseases					
Yes	60.5% (517/854)	Ref	56.8% (387/681)	0.1423	0.0810
Hypertensive disorders of pregnancy	17.2% (147/854)	Ref	18.2% (124/681)	0.6114	0.5726
GDM	12.8% (109/854)	Ref	11.9% (81/681)	0.6075	0.3867
Others†	43.8% (374/854)	Ref	38.9% (265/681)	0.0541	0.0366
Cesarean delivery	83.5% (695/832)	Ref	84.1% (571/679)	0.7687	0.9594
GA (weeks)	35.51 ± 3.95	Ref	35.91 ± 3.13	0.0180	0.0157
GA <28	4.2% (34/810)		3.0% (20/677)		
28 <32	3.5% (28/810)		4.3% (29/677)		
32 <34	8.8% (71/810)		6.8% (46/677)		
34 <37	36.8% (298/810)		34.3% (232/677)		
GA ≥37	46.8% (397/810)		51.7% (350/677)		
Apgar score <7 (1 and/or 5 min)	2.6% (41/1,579)	Ref	2.3% (31/1,338)	0.6278	0.5983
Birth weight (g)	2,449.74 ± 527.00	Ref	2,472.16 ± 557.28	0.2611	0.3320
<1,500	4.4% (68/1,559)		5.0% (67/1,335)		
1,500–2,499	42.3% (660/1,559)		37.6% (502/1,335)		
≥2,500	53.3% (831/1,559)		57.4% (766/1,335)		
Stillbirth					
n = 1	2.2% (18/801)	Ref	1.2% (8/673)	0.1304	0.1315
n = 2	2.6% (21/801)	Ref	1.5% (10/673)	0.1756	0.1864
Neonatal death					
n = 1	0.0% (0/801)	Ref	0.1% (1/673)	0.9915	0.9911
n = 2	0.2% (2/801)	Ref	0.0% (0/673)	0.9921	0.9914
NICU					
Yes	43.0% (684/1,590)	Ref	40.9% (552/1,348)	0.2659	0.1020
No	55.3% (879/1,590)	Ref	56.3% (759/1,348)	0.5912	0.3005
Gave up treatment	1.7% (27/1,590)	Ref	2.7% (37/1,348)	0.0554	0.0495
TTTS	1.6% (14/857)	Ref	1.6% (11/683)	0.9716	0.9455
FGR	2.7% (23/857)	Ref	3.4% (23/683)	0.4760	0.2749
sIUGR	1.2% (10/857)	Ref	1.3% (9/683)	0.7900	0.7632
Chorionicity diagnosis					
Yes	49.5% (424/857)	Ref	76.0% (519/683)	<0.0001	<0.0001
Ultrasound diagnosis (≤14 W)	25.2% (107/424)	Ref	29.5% (153/519)	<0.0001	0.1453
Postpartum diagnosis	60.6% (257/424)	Ref	57.0% (296/519)	<0.0001	<0.0001
Others‡	14.2% (60/424)	Ref	13.5% (70/519)	0.0235	0.0390

	2016 *n* = 752	*P*		2017 *n* = 706	*P*	
		Crude model	Adjusted model*		Crude model	Adjusted model*
Maternal age (years)	28.66 ± 4.22	0.0042	0.0042	29.17 ± 4.53	<0.0001	<0.0001
<20	1.5% (11/743)			1.6% (11/689)		
20–34	90.0% (669/743)			84.8% (584/689)		
≥35	8.5% (63/743)			13.6% (94/689)		
Parity		0.5698	0.5698		0.3721	0.3721

Contd...

Table 1: Contd...

	2016	*P*		2017	*P*	
	n = 752	Crude model	Adjusted model*	*n* = 706	Crude model	Adjusted model*
Primiparous	62.0% (466/752)			61.2% (430/703)		
Multiparous	38.0% (286/752)			38.8% (273/703)		
Pregnancy-related diseases						
Yes	67.8% (500/737)	0.0025	0.0033	69.6% (471/677)	0.0003	0.0008
Hypertensive disorders of pregnancy	16.1% (119/737)	0.5697	0.5502	15.7% (106/677)	0.4158	0.3136
GDM	15.5% (114/737)	0.1217	0.2008	17.0% (115/677)	0.0206	0.1025
Others†	51.7% (381/737)	0.0017	0.0011	54.5% (369/677)	<0.0001	<0.0001
Cesarean delivery	85.6% (635/742)	0.2632	0.4466	84.4% (580/687)	0.6377	0.9681
GA (weeks)	35.79 ± 3.31	0.0860	0.0892	36.11 ± 2.39	0.0004	0.0003
GA <28	1.9% (14/750)			1.0% (7/704)		
28 <32	4.7% (35/750)			4.4% (31/704)		
32 <34	6.0% (45/750)			5.8% (41/704)		
34 <37	41.6% (312/750)			37.1% (261/704)		
GA ≥37	45.9% (344/750)			51.7% (364/704)		
Apgar score <7 (1 and/or 5 min)	2.8% (38/1379)	0.7890	0.7611	2.3% (30/1,310)	0.5966	0.6824
Birth weight (g)	2,491.82 ± 552.60	0.0238	0.0426	2,509.21 ± 506.02	0.0025	0.0078
<1,500	5.0% (75/1,498)			4.4% (62/1,405)		
1,500–2,499	38.2% (572/1,498)			36.4% (512/1,405)		
≥2,500	56.8% (851/1,498)			59.1% (831/1,405)		
Stillbirth						
n = 1	0.9% (7/751)	0.0463	0.0465	1.4% (10/706)	0.2374	0.2715
n = 2	1.1% (8/751)	0.0426	0.0470	0.4% (3/706)	0.0042	0.0042
Neonatal death						
n = 1	0.1% (1/751)	0.9915	0.9910	0.1% (1/706)	0.9915	0.9909
n = 2	0.1% (1/751)	0.6458	0.6846	0.0% (0/706)	0.9920	0.9912
NICU						
Yes	43.4% (644/1,485)	0.7923	0.8195	37.4% (522/1,396)	0.0019	0.0032
No	54.1% (804/1,485)	0.5126	0.4873	61.5% (858/1,396)	0.0007	0.0012
Gave up treatment	2.5% (37/1,485)	0.1264	0.0989	1.1% (16/1,396)	0.2087	0.1706
TTTS	1.5% (11/752)	0.7823	0.9259	0.8% (6/706)	0.1776	0.2614
FGR	1.5% (11/752)	0.0942	0.1602	2.1% (15/706)	0.4760	0.7277
sIUGR	2.4% (18/752)	0.0660	0.0576	2.5% (18/706)	0.0454	0.0307
Chorionicity diagnosis						
Yes	88.0% (662/752)	<0.0001	<0.0001	93.5% (660/706)	<0.0001	<0.0001
Ultrasound diagnosis (≤14 W)	59.1% (391/662)	<0.0001	<0.0001	65.0% (429/660)	<0.0001	<0.0001
Postpartum diagnosis	21.1% (140/662)	<0.0001	<0.0001	20.5% (135/660)	<0.0001	<0.0001
Others‡	19.8% (131/662)	<0.0001	<0.0001	14.5% (96/660)	<0.0001	<0.0001

Data are shown as the mean ± SD or % (*n/N*). *Adjusted for maternal age, †Other pregnancy-related diseases include anemia, abnormal thyroid function, liver function damage, thrombocytopenia, ICP, placenta previa, and other diseases, ‡Patients with vague chorionicity diagnosis time (after 14 weeks GA) were classified into subgroup others. Ref: The data of 2014 was considered as reference data. NICU: Neonatal intensive care unit; TTTS: Twin-to-twin transfusion syndrome; FGR: Fetal growth restriction; sIUGR: Selective intrauterine growth restriction; SD: Standard deviation; ICP: Intrahepatic cholestasis of pregnancy; GA: Gestational age; GDM: Gestational diabetes mellitus.

difference within the incidence of TTTS (2015, *OR* = 0.83, 95% *CI* = 0.23–3.05; 2016, *OR* = 0.69, 95% *CI* = 0.18–2.67; 2017, *OR* = 0.13, 95% *CI* = 0.01–1.21) and rate of admission to the NICU (2015, *OR* = 0.77, 95% *CI* = 0.51–1.16; 2016, *OR* = 0.90, 95% *CI* = 0.59–1.35; 2017, *OR* = 0.94, 95% *CI* = 0.63–1.42). However, there was a statistical difference in the rate of admission to the NICU for MCMA and DCDA pregnancies, namely, there was a drop from 52.6% in 2014 to 21.9% in 2016 (MCDA, *OR* = 0.25; 95% *CI* = 0.09–0.71) and from 38.8% in 2014 to 30.5% in 2017 (DCDA, *OR* = 0.69; 95% *CI* = 0.55–0.87). Compared with 2014, the incidence of FGR in both MCMA and DCDA slightly decreased but did not make a statistical difference [Table 2].

For analysis of the risk factors of neonatal outcomes, we included hypertensive disorder complicating pregnancy and GDM because of their intimate relationship.[29-31] The results remained largely unchanged [Supplementary Tables 1 and 2].

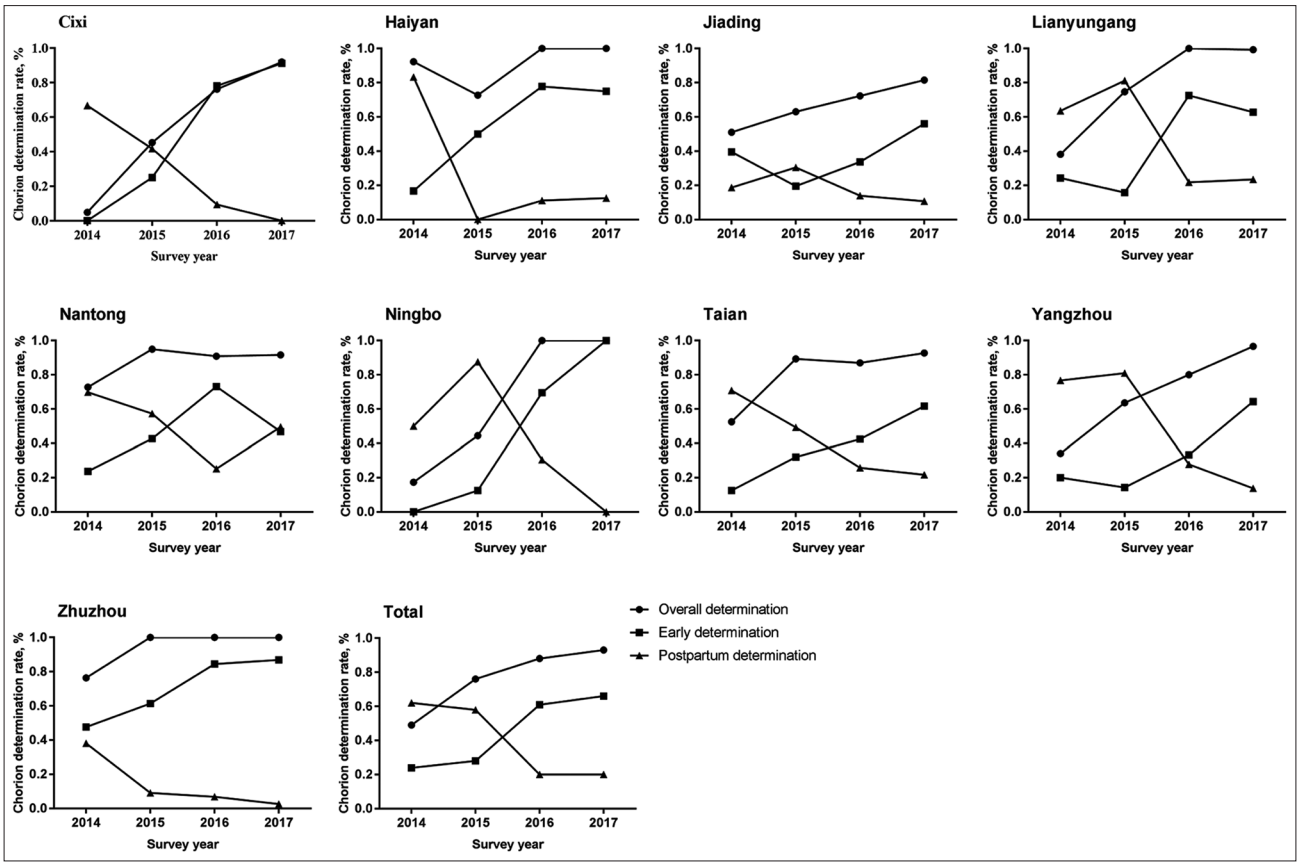

Figure 3: The rate of chorionicity determination in each center during 2014–2017.

Discussion

The study shows that clinical training in early chorionicity determination by ultrasonography in community hospitals has been practical and successful, facilitating prompt chorionicity diagnosis and preliminary screening for complications in twin pregnancy. The chorionicity determination rate approached 93.5% in community hospitals after the implementation of guidelines through clinical and ultrasound training. The early chorionicity determination rate increased from 25.2% in 2014 to 65.0% in 2017. We have shown that prompt chorionicity determination could also decrease the risk of preterm birth (GA <28 and 32≤ GA <34), and the latter may be due to a decreased rate of iatrogenic preterm labor in DCDA. This strategy also appeared to decrease the rate of stillbirth for one and two fetuses, and the risk of admission to the NICU. Increased early chorionicity determination rate may also reduce the risk of TTTS, but there was no significant difference, partly because of its low incidence originally. Interestingly, our data also showed that the incidence of sIUGR increased during the study years, which may result from more frequent surveillance after implementation of the guidelines. In conclusion, the implementation of professional guidelines is effective in a large-scale population. This motivates us to introduce further health policy guidelines.

We conducted this study in 12 community hospitals, 11 of which were concentrated in eastern coastal areas. The overall condition of chorionicity determination in other places in China needs further study. Besides, we need to invest more workforce for further guideline implementation. After 2-day training, primary physicians can also improve their clinical skills by continuous self-learning. More importantly, routine quality control was conducted every 3 months. It may take a long time to normalize the whole process of chorionicity determination; fortunately, we are glad to see that chorionicity determination rate approached 93.5% in 2017. In addition, the early chorionicity determination rate in 2017 declined in the Lianyungang and Nantong Women and Children's Hospitals. This may be due to insufficient supervision, indicating the critical importance of incorporating chorionicity determination by ultrasound in the first trimester into conventional diagnosis and treatment of twin pregnancy.

Strengths and limitations

Previous studies had suggested that the accuracy of amnionicity and chorionicity diagnosis was much higher in tertiary care centers than in referral providers, indicating a need for diagnostic skills in community hospitals to be enhanced. In addition, there had been a recommendation that referrals be made when the chorionicity determination was ambiguous.[13] Mackie *et al*. had specifically investigated the management of MC twins, exploring screening to predict complications in twin pregnancies.[32] To our knowledge, our study is the first to report and evaluate the effects of the implementation

Table 2: Subgroup analysis of pregnancy outcomes among MCDA, MCMA, and DCDA pregnancies

	2014		2015		
	n	*OR* (95% *CI*)	*n*	Crude model *OR* (95% *CI*)	Adjusted model* *OR* (95% *CI*)
MCDA					
Stillbirth					
n = 1	2.8% (2/72)	Ref	4.7% (6/129)	1.71 (0.34–8.69)	1.69 (0.33–8.61)
n = 2	4.2% (3/72)	Ref	0.8% (1/129)	0.18 (0.02–1.76)	0.18 (0.02–1.78)
NICU					
Yes	48.9% (68/139)	Ref	41.9% (106/253)	0.78 (0.52–1.18)	0.77 (0.51–1.16)
No	48.9% (68/139)	Ref	53.4% (135/253)	1.22 (0.82–1.85)	1.24 (0.83–1.88)
Gave up	2.2% (3/139)	Ref	4.7% (12/253)	2.29 (0.64–8.26)	2.27 (0.63–8.20)
FGR	2.8% (2/72)	Ref	6.2% (8/129)	2.31 (0.48–11.20)	2.32 (0.48–11.24)
TTTS	5.6% (4/72)	Ref	4.7% (6/129)	0.83 (0.23–3.04)	0.83 (0.23–3.05)
sIUGR	5.6% (4/72)	Ref	3.1% (4/129)	0.54 (0.13–2.24)	0.55 (0.13–2.28)
MCMA					
Stillbirth					
n = 1	5.3% (1/19)	Ref	0.0% (0/20)	–	–
n = 2	0.0% (0/19)	Ref	5.0% (1/20)	–	–
NICU					
Yes	52.6% (20/38)	Ref	45.0% (18/40)	0.82 (0.34–1.99)	0.72 (0.29–1.77)
No	47.4% (18/38)	Ref	50.0% (20/40)	1.00 (0.41–2.43)	0.89 (0.36–2.21)
Gave up	0.0% (0/38)	Ref	5.0% (2/40)	–	–
FGR	10.5% (2/19)	Ref	5.0% (1/20)	0.45 (0.04–5.39)	0.35 (0.03–4.75)
TTTS	5.3% (1/19)	Ref	5.0% (1/20)	0.95 (0.06–16.31)	0.95 (0.05–16.74)
sIUGR	5.3% (1/19)	Ref	5.0% (1/20)	0.95 (0.06–16.31)	1.07 (0.06–18.82)
DCDA					
Stillbirth					
n = 1	2.3% (6/261)	Ref	0.0% (0/297)	–	–
n = 2	1.1% (3/261)	Ref	1.7% (5/297)	1.47 (0.35–6.22)	1.49 (0.35–6.29)
NICU					
Yes	38.8% (198/510)	Ref	40.2% (238/592)	1.06 (0.83–1.35)	1.05 (0.82–1.34)
No	61.2% (312/510)	Ref	58.1% (344/592)	0.88 (0.69–1.12)	0.88 (0.69–1.13)
Gave up	0.0% (0/510)	Ref	1.7% (10/592)	–	–
FGR	2.3% (2/261)	Ref	2.0% (6/297)	0.88 (0.28–2.75)	0.88 (0.28–2.75)

	2016			2017		
	n	Crude model *OR* (95% *CI*)	Adjusted model* *OR* (95% *CI*)	*n*	Crude model *OR* (95% *CI*)	Adjusted model* *OR* (95% *CI*)
MCDA						
Stillbirth						
n = 1	3.1% (4/131)	1.10 (0.20–6.17)	1.08 (0.19-6.08)	0.7% (1/137)	0.26 (0.02–2.89)	0.26 (0.02–2.90)
n = 2	2.3% (3/131)	0.54 (0.11–2.74)	0.57 (0.11-2.90)	1.5% (2/137)	0.34 (0.06–2.09)	0.37 (0.06–2.29)
NICU						
Yes	45.6% (119/261)	0.93 (0.62–1.40)	0.90 (0.59-1.35)	46.7% (127/272)	0.97 (0.65–1.45)	0.94 (0.63–1.42)
No	47.5% (124/261)	1.00 (0.67–1.51)	1.05 (0.69–1.58)	51.5% (140/272)	1.17 (0.78–1.75)	1.19 (0.80–1.81)
Gave up	6.9% (18/261)	3.47 (1.00–11.98)	3.41 (0.99–11.82)	1.8% (5/272)	0.87 (0.21–3.71)	0.88 (0.21–3.73)
FGR	0.0% (0/131)	–	–	3.6% (5/137)	1.33 (0.25–7.01)	1.39 (0.26–7.41)
TTTS	3.8% (5/131)	0.68 (0.18–2.60)	0.69 (0.18–2.67)	0.7% (1/137)	0.13 (0.01–1.14)	0.13 (0.01–1.21)
sIUGR	3.1% (4/131)	0.54 (0.13–2.20)	0.56 (0.14–2.34)	5.8% (8/137)	1.05 (0.31–3.63)	1.16 (0.34–4.03)
MCMA						
Stillbirth						
n = 1	0.0% (0/17)	–	–	20.0% (3/15)	4.50 (0.42-48.53)	5.76 (0.51-64.81)
n = 2	5.9% (1/17)	–	–	0.0% (0/15)	–	–
NICU						

Contd...

Table 2: Contd...

	2016			2017		
	n	Crude model *OR* (95% *CI*)	Adjusted model* *OR* (95% *CI*)	*n*	Crude model *OR* (95% *CI*)	Adjusted model* *OR* (95% *CI*)
Yes	21.9% (7/32)	0.33 (0.12–0.93)	0.25 (0.09–0.71)	53.3% (16/30)	1.46 (0.54–3.94)	1.31 (0.47–3.70)
No	78.1% (25/32)	3.00 (1.08–8.34)	2.79 (1.00–7.80)	26.7% (8/30)	0.50 (0.02–1.39)	0.47 (0.16–1.37)
Gave up	0.0% (0/32)	–	–	6.7% (2/30)	–	–
FGR	5.9% (1/17)	0.53 (0.04–6.44)	0.48 (0.04–5.95)	6.7% (1/15)	0.61 (0.05–7.42)	0.50 (0.03–7.14)
TTTS	0.0% (0/17)	–	–	13.3% (2/15)	2.77 (0.23–33.88)	3.00 (0.24–38.10)
sIUGR	11.8% (2/17)	2.40 (0.20–29.13)	2.76 (0.22–34.74)	0.0% (0/15)	–	–
DCDA						
Stillbirth						
n = 1	0.5% (2/382)	0.22 (0.05–1.12)	0.24 (0.05–1.21)	0.5% (2/412)	0.21 (0.04–1.04)	0.24 (0.05–1.23)
n = 2	0.5% (2/382)	0.45 (0.08–2.73)	0.46 (0.08–2.75)	0.0% (0/412)	–	–
NICU						
Yes	36.6% (276/755)	0.91 (0.72–1.15)	0.92 (0.73–1.16)	30.5% (250/820)	0.69 (0.55–0.87)	0.69 (0.55–0.87)
No	62.8% (474/755)	1.07 (0.85–1.35)	1.06 (0.84–1.34)	69.1% (567/820)	1.42 (1.13–1.79)	1.42 (1.13–1.80)
Gave up	0.7% (5/755)	–	–	0.4% (3/820)	–	–
FGR	1.3% (5/382)	0.56 (0.17–1.87)	0.56 (0.17–1.84)	1.0% (4/412)	0.42 (0.12–1.49)	0.40 (0.11–1.43)

Ref, the data from 2014 were considered as reference data. If the absolute value of the data was zero, it was invalid in the statistical analysis, then the *OR* value was replaced by "–". Data are shown as % (*n/N*). *Adjusted for maternal age. *OR*: Odds ratio; *CI*: Confidence interval; MCDA: Monochorionic diamniotic; MCMA: Monochorionic monoamniotic; DCDA: Dichorionic diamniotic; NICU: Neonatal intensive care unit; TTTS: Twin-to-twin transfusion syndrome; FGR: Fetal growth restriction; sIUGR: Selective intrauterine growth restriction.

of pregnancy care guidelines as a management strategy on a national basis in any country.

Our study has limitations. Among patients who received chorionicity determination, those whose diagnosis time was not clear were classified into a subgroup of "others," which could incur biases in this study. However, the overall variation tendency of early and postpartum chorionicity determination rate was matched, indicating that the temporal tendency of primary outcomes after clinical training was credible. In our initial study design, we also included sensitivity and specificity of chorionicity determination by ultrasound as primary outcomes, taking postpartum diagnosis as a gold standard. However, the data of chorionicity diagnosis time derived from the twinning investigation handbook was recorded as GA either at ultrasound diagnosis or at delivery, so that we were unable to perform this part of the data analysis. We did not adjust for maternal body mass index (BMI) or smoking history because these data were not recorded completely. The improvements in pregnancy outcomes may be overestimated, whereas there was no influence on chorionicity determination rate, which was the primary outcome of this study. There was no relevant research about prepregnancy BMI and chorionicity, thus we ignore the influence of BMI on chorionicity determination.

In conclusion, the implementation of guidelines on chorionicity determination was beneficial for improving chorionicity determination rates and relative pregnancy outcomes. It developed approaches to translating clinical guidelines into practice. Regular training workshops of obstetric care are recommended as part of health policy and guideline implementation to further decrease maternal and neonatal mortality and morbidity.

Supplementary information is linked to the online version of the paper on the Reproductive and Developmental Medicine website.

Acknowledgments

The authors are thankful to members of staff in Cixi Women and Children's Hospital; Haiyan Women and Children's Hospital; Jiading Women and Children's Hospital; Lianyungang Women and Children's Hospital; Nantong Women and Children's Hospital; The Forth People's Hospital of Ningbo; Taian Women and Children's Hospital; Yangzhou Women and Children's Hospital; Zhuzhou Women and Children's Hospital; Xuzhou Women and Children's Hospital; Kunshan Women and Children's Hospital; and The First People's Hospital of Kunshan.

Financial support and sponsorship

This program was supported by the Shanghai Key Program of Clinical Science and Technology Innovation (17411950500; 17411950501; 18511105602), National Science Foundation of China (81741047; 81971411), Shanghai Medical Center of Key Programs for Female Reproductive Diseases (2017ZZ01016), National Key Basic Research Plan of China (973 Plan) (2015CB943300), and The Major Program of the National 13th Five-Year Plan of China (2016YFC1000400).

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Sensitivity analysis with exclusion of data with no maternal age

	2014 *n* = 825	*P*	2015 *n* = 660	Sensitivity analysis *P*
Pregnancy-related diseases				
Yes	60.6% (500/825)	Ref	56.2% (371/660)	0.0811
Hypertensive disorder complicating pregnancy	17.1% (141/825)	Ref	18.3% (121/660)	0.5727
GDM	12.7% (105/825)	Ref	11.5% (76/660)	0.3868
Others*	43.9% (362/825)	Ref	38.3% (253/660)	0.0366
Cesarean delivery	83.7% (671/802)	Ref	83.9% (553/659)	0.9594
GA (week)	35.47 ± 4.00	Ref	35.90 ± 3.16	0.0157
GA <28	4.4% (34/781)		3.0% (20/657)	
28≤ GA <32	3.6% (28/781)		4.3% (28/657)	
32≤ GA <34	8.3% (65/781)		6.8% (45/657)	
34≤ GA <37	37.6% (294/781)		33.9% (223/657)	
GA ≥37	46.1% (360/781)		51.9% (341/657)	
Apgar score <7 (1 or 5 min)	2.6% (40/1,521)	Ref	2.3% (30/1,298)	0.5983
Birth weight (g)	2447.72 ± 529.56	Ref	2469.03 ± 560.01	0.3320
<1,500	4.5% (67/1,501)		5.1% (66/1,295)	
1,500–2,499	42.2% (634/1,501)		38.0% (492/1,295)	
≥2,500	53.3% (800/1,501)		56.9% (737/1,295)	
Stillbirth				
n = 1	2.3% (18/772)	Ref	1.2% (8/653)	0.1315
n = 2	2.7% (21/772)	Ref	1.5% (10/653)	0.1864
Neonatal death				
n = 1	0.0% (0/772)	Ref	0.2% (1/653)	0.9909
n = 2	0.3% (2/772)	Ref	0.2% (1/653)	0.9914
NICU				
Yes	43.2% (662/1531)	Ref	40.1% (525/1308)	0.1062
No	55.0% (842/1531)	Ref	57.0% (746/1308)	0.3093
Give up treatment	1.8% (27/1531)	Ref	2.8% (37/1308)	0.0498
TTTS	1.6% (13/826)	Ref	1.5% (10/660)	0.9455
FGR	2.5% (21/826)	Ref	3.5% (23/660)	0.2749
sIUGR	1.2% (10/826)	Ref	1.4% (9/660)	0.7632
	2016 *n* = 743	**Sensitivity analysis *P***	**2017 *n* = 689**	**Sensitivity analysis *P***
Pregnancy-related diseases				
Yes	68.0% (495/728)	0.0033	69.4% (458/660)	0.0008
Hypertensive disorder complicating pregnancy	16.2% (118/728)	0.5503	15.6% (103/660)	0.3136
GDM	15.5% (113/728)	0.2008	17.0% (112/660)	0.1026
Others*	51.8% (377/728)	0.0011	54.2% (358/660)	<0.0001
Cesarean delivery	85.4% (626/733)	0.4466	84.4% (566/671)	0.9681
GA (week)	35.78 ± 3.32	0.0892	36.13 ± 2.34	0.0003
GA <28	1.9% (14/741)		0.9% (6/687)	
28≤ GA <32	4.7% (35/741)		4.5% (31/687)	
32≤ GA <34	6.1% (45/741)		5.8% (40/687)	
34≤ GA <37	41.7% (309/741)		36.8% (253/687)	
GA ≥37	45.6% (338/741)		52.0% (357/687)	
Apgar score <7 (1 or 5 min)	2.8% (38/1,361)	0.7611	2.3% (30/1,278)	0.6824
Birth weight (g)	2492.10 ± 550.26	0.0426	2510.19 ± 502.92	0.0078
<1,500	5.1% (75/1,480)		4.4% (60/1,371)	
1,500–2,499	38.3% (567/1,480)		36.5% (500/1,371)	
≥2,500	56.6% (838/1,480)		59.2% (811/1,371)	
Stillbirth				
n = 1	0.9% (7/742)	0.0465	1.5% (10/689)	0.2715
n = 2	1.1% (8/742)	0.0470	0.3% (2/689)	0.0042

Contd...

Supplementary Table 1: Contd...

	2016 *n* = 743	Sensitivity analysis *P*	2017 *n* = 689	Sensitivity analysis *P*
Neonatal death				
n = 1	0.1% (1/742)	0.9910	0.1% (1/689)	0.9911
n = 2	0.0% (0/742)	0.6846	0.0% (0/689)	0.9912
NICU				
Yes	43.4% (637/1,467)	0.8042	37.4% (509/1,362)	0.0034
No	54.1% (793/1,467)	0.4755	61.6% (839/1,362)	0.0013
Give up treatment	2.5% (37/1,467)	0.0995	1.0% (14/1,362)	0.1699
TTTS	1.5% (11/743)	0.9259	0.9% (6/689)	0.2614
FGR	1.5% (11/743)	0.1602	2.2% (15/689)	0.7277
sIUGR	2.4% (18/743)	0.0576	2.6% (18/689)	0.0307

Data are shown as mean ± SD or % (*n/N*). *Other pregnancy-related diseases include anemia, abnormal thyroid function, liver function damage, thrombocytopenia. ICP: placenta previa and other diseases; NICU: Neonatal intensive care unit; TTTS: Twin-to-twin transfusion syndrome; FGR: Fetal growth restriction; sIUGR: Selective intrauterine growth restriction; SD: Standard deviation; GA: Gestational age; GDM: Gestational diabetes mellitus; Ref, the data from 2014 were considered as reference data.

Supplementary Table 2: Sensitivity analysis adjusted for hypertensive disorders complicating pregnancy and GDM

	2014 *n* = 857	*P*	2015 *n* = 683	Sensitivity analysis *P*
Cesarean delivery	83.5% (695/832)	Ref	84.1% (571/679)	0.9953
GA (week)	35.51 ± 3.95	Ref	35.91 ± 3.13	0.0209
GA <28	4.2% (34/810)		3.0% (20/677)	
28≤ GA <32	3.5% (28/810)		4.3% (29/677)	
32 ≤GA <34	8.8% (71/810)		6.8% (46/677)	
34 ≤GA <37	36.8% (298/810)		34.3% (232/677)	
GA ≥37	46.8% (397/810)		51.7% (350/677)	
Apgar score <7 (1 or 5 min)	2.6% (41/1579)	Ref	2.3% (31/1338)	0.5828
Birth weight (g)	2449.74 ± 527.00	Ref	2472.16 ± 557.28	0.3210
<1,500	4.4% (68/1,559)		5.0% (67/1,335)	
1,500–2,499	42.3% (660/1,559)		37.6% (502/1,335)	
≥2,500	53.3% (831/1,559)		57.4% (766/1,335)	
Stillbirth				
n = 1	2.2% (18/801)	Ref	1.2% (8/673)	0.1364
n = 2	2.6% (21/801)	Ref	1.5% (10/673)	0.2365
Neonatal death				
n = 1	0.0% (0/801)	Ref	0.1% (1/673)	0.9908
n = 2	0.2% (2/801)	Ref	0.0% (0/673)	0.9910
NICU				
Yes	43.0% (684/1,590)	Ref	40.9% (552/1,348)	0.1224
No	55.3% (879/1,590)	Ref	56.3% (759/1,348)	0.3455
Give up treatment	1.7% (27/1,590)	Ref	2.7% (37/1,348)	0.0506
TTTS	1.6% (14/857)	Ref	1.6% (11/683)	0.9411
FGR	2.7% (23/857)	Ref	3.4% (23/683)	0.2971
sIUGR	1.2% (10/857)	Ref	1.3% (9/683)	0.7596
	2016 *n* = 752	**Sensitivity analysis *P***	**2017 *n* = 706**	**Sensitivity analysis *P***
Cesarean delivery	85.6% (635/742)	0.4816	84.4% (580/687)	0.8998
GA (week)	35.79 ± 3.31	0.1323	36.11 ± 2.39	0.0010
GA <28	1.9% (14/750)		1.0% (7/704)	
28≤ GA <32	4.7% (35/750)		4.4% (31/704)	
32 ≤GA <34	6.0% (45/750)		5.8% (41/704)	
34 ≤GA <37	41.6% (312/750)		37.1% (261/704)	
GA ≥37	45.9% (344/750)		51.7% (364/704)	

Contd...

Supplementary Table 2: Contd...

	2016 *n* = 752	Sensitivity analysis *P*	2017 *n* = 706	Sensitivity analysis *P*
Apgar score <7 (1 or 5 min)	2.8% (38/1,379)	0.7989	2.3% (30/1,310)	0.7949
Birth weight (g)	2491.82 ± 552.60	0.0660	2509.21 ± 506.02	0.0254
<1,500	5.0% (75/1,498)		4.4% (62/1,405)	
1,500–2,499	38.2% (572/1,498)		36.4% (512/1,405)	
≥2,500	56.8% (851/1,498)		59.1% (831/1,405)	
Stillbirth				
n = 1	0.9% (7/751)	0.0521	1.4% (10/706)	0.3318
n = 2	1.1% (8/751)	0.0708	0.4% (3/706)	0.0060
Neonatal death				
n = 1	0.1% (1/751)	0.9907	0.1% (1/706)	0.9906
n = 2	0.1% (1/751)	0.6625	0.0% (0/706)	0.9911
NICU				
Yes	43.4% (644/1,485)	0.7503	37.4% (522/1,396)	0.0145
No	54.1% (804/1,485)	0.4236	61.5% (858/1,396)	0.0064
Give up treatment	2.5% (37/1,485)	0.0922	1.1% (16/1,396)	0.1964
TTTS	1.5% (11/752)	0.9677	0.8% (6/706)	0.3066
FGR	1.5% (11/752)	0.1955	2.1% (15/706)	0.7360
sIUGR	2.4% (18/752)	0.0666	2.5% (18/706)	0.0273

Data are shown as mean ± SD or % (*n/N*). NICU: Neonatal intensive care unit; TTTS: Twin-to-twin transfusion syndrome; FGR: Fetal growth restriction; sIUGR: Selective intrauterine growth restriction; SD: Standard deviation; GA: Gestational age; GDM: Gestational diabetes mellitus; Ref, the data from 2014 were considered as reference data.