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Changes in the perinatal outcomes of twin pregnancies delivered at a tertiary referral center in Korea during a 24-year period from 1995 to 2018

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Objective
To analyze the changes in the clinical characteristics and perinatal outcomes of twin pregnancies delivered at a tertiary referral center in Korea during a 24-year period.

Methods
This was a retrospective cohort study of twin pregnancies delivered at 24–40 weeks of gestation, from 1995 to 2018. The subjects were divided into 4 groups according to the year of delivery: 1995–2000, 2001–2006, 2007–2012, and 2013–2018. The trends in the changes in the twin birth rate, maternal age, assisted reproductive technology (ART) pregnancy rate, chorionicity, obstetric complications, delivery outcomes, and neonatal outcomes over the periods were analyzed.

Results
A total of 2,133 twin pregnancies were included in the study. The twin birth rate increased from 16.7/1,000 in 1995–2000 to 42.2/1,000 in 2001–2006, 49.5/1,000 in 2007–2012, and 61.8/1,000 in 2013–2018. The maternal age and ART pregnancy and dichorionic twin rates increased, while the monochorionic twin rate decreased over the periods. The incidence of fetal congenital anomalies, cervical incompetence, gestational diabetes mellitus, preeclampsia, and placental abruption increased over the periods. The preterm birth (PTB) rate significantly decreased owing to the decreasing elective late-PTB rate; however, the early-PTB rate significantly increased.

Conclusion
This study found that twin pregnancies increased steadily over the last 24 years and that the increase was related to increased maternal age and ART pregnancy rate. The incidence of obstetric complications increased over the periods; however, the neonatal intensive care unit admission rate decreased, along with decreases in the elective late-PTB rate.

Keywords: Twin pregnancy; Obstetric complications; Delivery

Introduction

The twin pregnancy rates are increasing worldwide. In the United States (US), the twin pregnancy rate has rapidly increased from 1.89% in 1980 to 3.34% in 2016 [1]. According to the birth statistics assessed by the Korea Institute for Health and Social Affairs, the multiple pregnancy rate increased from 2.02% in 2003 to 3.80% in 2016 [2]. The increasing trend in multiple pregnancies is attributed to older maternal age at childbirth and the increased use of assisted reproductive technology (ART) [3].

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A twin pregnancy is associated with an increased risk of many maternal complications, such as preterm delivery, gestational diabetes mellitus (GDM), and preeclampsia. One study found that women with twin pregnancies were 6 times more likely to be hospitalized owing to obstetric complications than those with singleton pregnancies [4]. A twin pregnancy is also a risk factor for various neonatal complications, such as stillbirth, fetal growth restriction, low birth weight, neonatal death, and other neonatal morbidities [4-6].

Many studies have been conducted on multiple pregnancies under various clinical settings, including a simple comparison between twin and singleton pregnancies, comparison between twin pregnancies conceived via ART and natural twin pregnancies, and investigations according to the chorionicity of twins [7-9]. However, changes in the characteristics and perinatal outcomes of twin pregnancies over a long period have not been extensively studied in the Korean population. Therefore, the objective of this study was to investigate the changes in the clinical characteristics and maternal and neonatal outcomes of twin pregnancies during a 24-year period, from 1995 to 2018, at a tertiary academic hospital.

Materials and methods

This was a retrospective cohort study of all consecutive twin pregnancies delivered at ≥24 weeks of gestation at a tertiary academic hospital in Seoul, Korea, from 1995 to 2018. Cases of death of 1 or both fetuses in utero before 24 weeks of gestation and triplet or higher multiple pregnancies were excluded from the analysis. Maternal characteristics, obstetric complications, delivery outcomes, and neonatal outcomes were retrieved from the medical records. The subjects were categorized into 4 period groups according to the year of delivery: 1995–2000 (period 1), 2001–2006 (period 2), 2007–2012 (period 3), and 2013–2018 (period 4).

The maternal characteristics evaluated included maternal age, parity, type of conception (spontaneous or ART), and chorionicity. Advanced maternal age was defined as an age of ≥35 years. Maternal age was further categorized into 5 groups: <25, 25–29, 30–34, 35–39, or ≥40 years. Chorionicity was determined by sonographic findings in the first or early second trimester, such as the number of gestational sacs and placenta, presence of the twin peak or T sign, and fetal sex. Macroscopic and pathological examination of the placenta confirmed the chorionicity after delivery.

The obstetric complications included twin-to-twin transfusion syndrome (TTTS), fetal death in utero (FDIU), birth weight discordance, major congenital anomalies, preterm labor, incompetent internal os of the cervix (IIOC), preterm premature rupture of membranes (PPROM), preeclampsia, GDM, placental abruption, and placenta previa. GDM was diagnosed when 2 or more glucose values were above the National Diabetes Plasma Data Group (NDDG) criteria (fasting, 1-hour, 2-hour, and 3-hour plasma glucose levels of 105, 190, 165, and 145 mg/dL, respectively) or Carpenter and Coustan criteria (fasting, 1-hour, 2-hour, and 3-hour plasma glucose levels of 95, 180, 155, and 140 mg/dL, respectively). Birth weight discordance was defined as inter-twin weight discordance of more than 20%. Major congenital anomalies were defined as anomalies that required medical or surgical interventions after birth. IIOC was defined as the painless protrusion of the amniotic membrane through the uterine cervix.

The delivery outcomes included the gestational age at delivery, mode of delivery, and indications for delivery. The gestational age at delivery was categorized as early preterm ($24^{0/7}$–$33^{6/7}$ weeks of gestation), late preterm ($34^{0/7}$–$36^{6/7}$ weeks of gestation), and term (≥ $37^{0/7}$ weeks of gestation). The mode of delivery was classified as vaginal delivery of both twins, cesarean section delivery of both twins, and first twin vaginal-second twin cesarean delivery. The indications for early preterm delivery were preterm labor, PPROM, or maternal-fetal indications. The indications for late preterm delivery were preterm labor, PPROM, maternal-fetal indications, or elective delivery. The indications for term delivery were spontaneous labor, premature rupture of membrane (PROM), maternal-fetal indications, or elective delivery. Elective delivery was defined as labor induction or cesarean delivery without any identifiable medical indication. Maternal-fetal indications referred to obstetric or medical complications, including preeclampsia, GDM, fetal growth restriction, fetal congenital anomalies, placenta previa, and placental abruption.

The neonatal outcome measures included sex, birth weight, small for gestational age (SGA), Apgar scores, admission to the neonatal intensive care unit (NICU), duration of the NICU stay, requirement for mechanical ventilator support, duration of mechanical ventilation therapy, mortality, and neonatal morbidities. The neonatal morbidities analyzed were respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), transient tachypnea of newborn (TTN), grade 3–4 intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), stage 2–3 necrotizing enterocolitis (NEC), early and late neonatal sepsis, and grade 3–4 retinopathy of prematurity (ROP). SGA, as described in the neonatal medical records, was defined as the condition in which the infant birth weight was lower than the 10th percentile for gestational age. RDS was diagnosed if the following were present: respiratory grunting and retracting, increased oxygen requirement (FiO_2 of >0.4), and ground-glass appearance and air bronchograms on simple chest radiography. BPD was defined as the condition in which supplementary oxygen was needed for ≥28 days or by diagnostic radiographic or histological findings. IVH was diagnosed using brain ultrasonography and graded using the Papile classification system for intraventricular bleeding without (grade 2) or with ventricular dilatation (grade 3) or with parenchymal involvement (grade 4). PVL was defined as the presence of a cystic lesion and echogenicity in the periventricular white matter. ROP was graded using the International Classification of ROP. NEC was defined in accordance with the modified Bell's staging criteria as acquired neonatal acute intestinal necrosis of unknown etiology. Neonatal sepsis was diagnosed on the basis of positive blood culture findings (proven sepsis) or positive laboratory evidence in neonates clinically suspected to have sepsis (suspected sepsis).

The data obtained were analyzed using the Statistical Package for Social Sciences version 24 (SPSS Statistics; IBM, Armonk, NY, US). The maternal characteristics, obstetric complications, delivery outcomes and indications, and neonatal outcomes were compared across the 4 periods. The trends were analyzed using the Jonckheere-Terpstra test for continuous variables and a linear-by-linear association analysis for categorical variables. *P*-values of <0.05 were considered statistically significant.

Results

A total of 2,133 twin pregnancies were delivered at our institution during the 24-year study period. The twin birth

Table 1. Maternal characteristics

Characteristics	Period 1 (1995–2000) (n=371)	Period 2 (2001–2006) (n=608)	Period 3 (2007–2012) (n=599)	Period 4 (2013–2018) (n=555)	*P*-value[a)]
Age (yr)	30.78±4.01	31.27±3.90	32.46±3.63	33.56±3.53	<0.001
<25	15 (4.0)	16 (2.6)	11 (1.8)	5 (0.9)	<0.001
25–29	141 (38.0)	184 (30.3)	111 (18.5)	56 (10.1)	
30–34	144 (38.8)	302 (49.7)	301 (50.3)	288 (51.9)	
35–39	3 (17.0)	91 (15.0)	159 (26.5)	180 (32.4)	
≥40	8 (2.2)	15 (2.5)	17 (2.8)	26 (4.7)	
Parity					
Nulliparous	263 (70.9)	470 (77.3)	443 (74.0)	446 (80.4)	0.008
Multiparous	108 (29.1)	138 (22.7)	156 (26.0)	109 (19.6)	
Prior preterm delivery history	14 (3.8)	22 (3.6)	23 (3.8)	20 (3.6)	0.952
ART	123 (33.2)	283 (46.5)	304 (50.8)	345 (62.2)	<0.001
Chorionicity					
MCMA	6 (1.7)	2 (0.3)	4 (0.7)	0 (0)	<0.001
MCDA	128 (36.6)	171 (28.2)	123 (20.5)	92 (16.6)	
DCDA	216 (61.7)	433 (71.5)	472 (78.8)	463 (83.4)	

Data expressed as mean±standard deviation or number (%).
ART, artificial reproductive technology; MCMA, monochorionic monoamniotic; MCDA, monochorionic diamniotic; DCDA, dichorionic diamniotic.
[a)]Jonckheere-Terpstra test for continuous variables and linear-by-linear association for categorical variables.

rate increased from 16.7/1,000 in 1995–2000 (period 1) to 42.2/1,000 in 2001–2006 (period 2), 49.5/1,000 in 2007–2012 (period 3), and 61.8/1,000 in 2013–2018 (period 4). The mean maternal age and the number of women with advanced maternal age significantly increased from period 1 to period 4 (Table 1). More specifically, the incidence of twin pregnancies in the women aged under 25 and 25–29 years significantly decreased from period 1 to period 4, while that in the women aged 30–34, 35–39, and ≥40 years significantly increased. The rate of twin pregnancies conceived via ART rapidly increased from period 1 to period 4 (33.2% vs. 46.5% vs. 50.8% vs. 62.2% in periods 1, 2, 3, and 4, respectively, *P*<0.001). The proportion of dichorionic twin pregnancies increased from period 1 to period 4, while the proportion of monochorionic twin pregnancies decreased.

The rates of obstetric complications, including FDIU, TTTS,

Table 2. Obstetric complications

Characteristics	Period 1 (1995–2000) (n=371)	Period 2 (2001–2006) (n=608)	Period 3 (2007–2012) (n=599)	Period 4 (2013–2018) (n=555)	*P*-value[a)]
One or both FDIU	9 (2.4)	12 (2.0)	9 (1.5)	9 (1.6)	0.320
One or both fetal anomaly	11 (3.0)	22 (3.6)	39 (6.5)	59 (10.6)	<0.001
TTTS	2 (0.5)	12 (2.0)	17 (2.8)	9 (1.6)	0.229
Preterm labor	117 (31.5)	223 (36.7)	207 (34.6)	188 (33.9)	0.830
IIOC	4 (1.1)	2 (0.3)	18 (3.0)	30 (5.4)	<0.001
PPROM	58 (15.6)	113 (18.6)	107 (17.9)	114 (20.5)	0.098
Preeclampsia	27 (7.3)	56 (9.2)	73 (12.2)	63 (11.4)	0.019
Gestational diabetes	5 (2.4)	24 (4.8)	45 (8.3)	60 (11.7)	<0.001
NDDG criteria[b)]	5 (2.4)	21 (4.2)	21 (4.0)	35 (7.2)	0.005
C&C criteria[b)]	8 (3.8)	27 (5.4)	30 (5.8)	48 (9.9)	0.001
Placenta abruption	6 (1.6)	14 (2.3)	20 (3.3)	21 (3.8)	0.028
Placenta previa	5 (1.3)	14 (2.3)	15 (2.5)	16 (2.9)	0.147
Birth weight discordancy	70 (19.0)	118 (19.4)	125 (20.9)	114 (20.5)	0.455

Data expressed as number (%).

FDIU, fetal death in utero; TTTS, twin-to-twin transfusion syndrome; IIOC, incompetent internal os of cervix; PPROM, preterm premature rupture of membranes; NDDG, National Diabetes Data Group; C&C, Carpenter & Coustan.

[a)]Jonckheere-Terpstra test for continuous variables and linear-by-linear regression for categorical variables; [b)]Women with all 4 blood sugar levels were available were analyzed only.

Table 3. Delivery outcome

Characteristics	Period 1 (1995–2000) (n=371)	Period 2 (2001–2006) (n=608)	Period 3 (2007–2012) (n=599)	Period 4 (2013–2018) (n=555)	*P*-value[a)]
Gestational age at delivery (wk)	35.2±2.7	34.7±3.2	34.7±3.7	34.9±3.7	0.002
Early-preterm	82 (22.1)	172 (28.3)	169 (28.2)	151 (27.2)	<0.001
Late-preterm	205 (55.3)	284 (46.7)	187 (31.2)	159 (28.6)	
Term	84 (22.6)	152 (25.0)	243 (40.6)	245 (44.1)	
Mode of delivery					
Both vaginal delivery	8 (2.2)	58 (9.5)	87 (14.5)	60 (10.8)	<0.001
Both cesarean section	361 (97.3)	549 (90.3)	507 (84.6)	490 (88.3)	
First twin vaginal delivery-second twin cesarean	2 (0.5)	1 (0.2)	5 (0.8)	5 (0.9)	

Data expressed as mean±standard deviation or number (%).

[a)]Jonckheere-Terpstra test for continuous variables and linear-by-linear regression for categorical variables.

preterm labor, PPROM, placenta previa, and discordant twins, were similar across the 4 periods (Table 2). However, the rates of fetal congenital anomalies, IIOC, preeclampsia, and placental abruption significantly increased from period 1 to period 4. The rate of GDM significantly increased from period 1 to period 4, and this pattern was similar when either the NDDG standards or the Carpenter and Coustan standards were applied as the diagnostic criteria.

The mean gestational age at delivery significantly decreased from period 1 to period 4 (Table 3). The early preterm birth rate and term birth rate significantly increased; however, the late preterm birth rate significantly decreased from period 1 to period 4. The rate of twin cesarean sections decreased gradually, and the rate of twin vaginal deliveries significantly increased from period 1 to period 4.

At early preterm gestation, the rate of preterm labor tended to decrease, while the rate of deliveries owing to maternal-fetal indications tended to increase from period 1 to period 4 (Table 4). At late preterm gestation, the rate of elective delivery significantly decreased from 49.8% in period 1 to 11.9% in period 4, while the rate of preterm labor, PPROM, and maternal-fetal delivery indications tended to increase over the periods. At term gestation, elective delivery was the most common indication. The rates of spontaneous labor, PROM, maternal-fetal delivery indications, and elective deliveries did not change significantly across the 4 periods.

The neonatal outcomes, including sex, birth weight, neonatal and infant mortalities, IVH (≥grade 3), ROP (≥grade 3), NEC (≥stage 2), and early and late sepsis, were similar across the 4 periods (Table 5). The rate of neonates having low Apgar scores (1-minute Apgar score of <4 or 5-minute Apgar score of <7) decreased from period 1 to period 4. The rate of NICU admissions decreased; however, the mean NICU stay duration increased from period 1 to period 4. The rates of SGA, PDA, and PVL increased from period 1 to period 4, and those of respiratory complications and related factors, including RDS, BPD, TTN, need for ventilator treatment, and duration of assisted ventilation, increased significantly.

Discussion

In this study, we analyzed changes in the perinatal outcomes of twin pregnancies at a tertiary referral center from 1995 to 2018. We found that the twin birth rate increased during the study period in association with an increase in maternal

Table 4. Indications for delivery at early preterm, late preterm and term gestation

Characteristics	Period 1 (1995–2000)	Period 2 (2001–2006)	Period 3 (2007–2012)	Period 4 (2013–2018)	*P*-value[a)]
Early preterm	(n=82)	(n=172)	(n=169)	(n=151)	
PTL	49 (59.8)	95 (55.2)	97 (57.4)	66 (43.7)	0.010
PPROM	27 (32.9)	55 (32.0)	43 (25.4)	60 (39.7)	
Maternal-fetal indication	6 (7.3)	22 (12.8)	29 (17.2)	25 (16.6)	
Late preterm	(n=205)	(n=284)	(n=187)	(n=159)	
PTL	42 (20.5)	58 (20.4)	61 (32.6)	47 (29.6)	<0.001
PPROM	30 (14.6)	55 (19.4)	60 (32.1)	52 (32.7)	
Maternal-fetal indication	31 (15.1)	45 (15.8)	36 (19.3)	41 (25.8)	
Elective	102 (49.8)	126 (44.4)	30 (16.0)	19 (11.9)	
Term	(n=84)	(n=152)	(n=243)	(n=245)	
Spontaneous labor	4 (4.8)	11 (7.2)	19 (7.8)	8 (3.3)	0.171
PROM	4 (4.8)	9 (5.9)	12 (4.9)	8 (3.3)	
Maternal-fetal indication	6 (7.1)	12 (7.9)	21 (8.6)	19 (7.8)	
Elective	70 (83.3)	120 (78.9)	191 (78.6)	210 (85.7)	

Data expressed as number (%).
PTL, preterm labor; PPROM, preterm premature rupture of membranes; PROM, premature rupture of membranes.
[a)]Linear-by-linear regression.

age and the rate of ART twin pregnancies. Our results agree with recent US and European epidemiological study results [8]. The increase in the rate of ART twin pregnancies was likely associated with the increased marriage age of women, which is probably a result of women's increased participation in society, as well as advances in ART and increasing government support for ART. Such an increase also led to changes in the chorionicity of twin pregnancies. In our study, the proportion of dichorionic twin pregnancies increased, while the proportion of monochorionic twin pregnancies decreased across the study periods.

Monochorionic twins are known to have higher risks of fetal congenital anomalies, preterm birth, fetal growth retardation, discordant twins, and FDIU than dichorionic twins [10,11]. However, despite the decrease in the proportion of monochorionic twins in our study population, the rates of fetal congenital anomalies and SGA increased significantly. The rates of discordant twins and FDIU did not change over the periods. The increases in the rates of fetal congenital anomalies might be attributed to other factors. Several clinical studies reported that ART increased the risk of congenital anomalies [12,13]; however, other reports found a lack of association between ART and fetal congenital anomalies [14,15]. Therefore, whether an increase in the use of ART is associated with an increase in the rates of fetal congenital anomalies is still controversial. The increase in maternal age might be another factor associated with increases in the rates of fetal congenital anomalies [16]. However, the most

Table 5. Neonatal outcomes[a)]

Characteristics	Period 1 (1995–2000) (n=740)	Period 2 (2001–2006) (n=1,216)	Period 3 (2007–2012) (n=1,198)	Period 4 (2013–2018) (n=1,109)	*P*-value[b)]
Sex (male)	398 (54.3)	613 (50.9)	641 (54.0)	537 (48.8)	0.082
Birth weight (kg)	2.21±0.52	2.13±0.60	2.14±0.68	2.16±0.66	0.365
SGA	71 (9.7)	108 (9.0)	126 (10.6)	235 (21.3)	<0.001
1-min Apgar score <4	48 (6.5)	79 (6.6)	28 (2.4)	34 (3.1)	<0.001
5-min Apgar score <7	59 (8.0)	67 (5.6)	32 (2.7)	45 (4.1)	<0.001
NICU admission	387 (52.8)	589 (48.9)	473 (39.8)	430 (39.1)	<0.001
Duration of NICU stay (days)	14 (1–284)	19 (1–226)	30 (1–547)	26 (1–482)	<0.001
Ventilator treatment	133 (18.1)	238 (19.8)	258 (21.7)	252 (22.9)	0.007
Duration of assisted ventilation (days)	5 (1–284)	4 (1–92)	13 (1–547)	9.5 (1–482)	<0.001
Mortality	12 (1.6)	27 (2.2)	21 (1.8)	26 (2.4)	0.472
Neonatal morbidity					
RDS	80 (10.9)	186 (15.4)	191 (16.1)	199 (18.1)	<0.001
BPD	26 (3.5)	52 (4.3)	92 (7.8)	90 (8.2)	<0.001
TTN	38 (5.2)	39 (3.2)	15 (1.3)	19 (1.7)	<0.001
IVH (≥grade 3)	6 (0.8)	13 (1.1)	21 (1.8)	16 (1.5)	0.132
PVL	4 (0.5)	10 (0.8)	15 (1.3)	25 (2.3)	<0.001
PDA	68 (9.3)	175 (14.5)	141 (11.9)	156 (14.2)	0.046
ROP (≥grade 3)	17 (2.3)	31 (2.6)	22 (1.9)	31 (2.8)	0.743
NEC (≥stage 2)	8 (1.1)	13 (1.1)	36 (3.0)	18 (1.6)	0.062
Early sepsis	41 (5.6)	69 (5.8)	78 (6.6)	43 (3.9)	0.149
Late sepsis	31(4.2)	53(4.4)	66(5.6)	30 (2.7)	0.193

Data expressed as mean±standard deviation or median (range) or number (%).
SGA, small-for-gestational age; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; BPD, bronchopulmonary dysplasia; TTN, transient tachypnea of newborn; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; NEC, necrotizing enterocolitis.
[a)]Fetal death cases were excluded and only live born babies were included in the analysis; [b)]Jonckheere-Terpstra test for continuous variables and linear-by-linear regression for categorical variables.

important reason for the increased rates of fetal congenital anomalies may be advances in ultrasonographic imaging technology and improvements in the prenatal diagnoses and referral of fetal congenital anomalies at our tertiary referral center. The types of fetal congenital anomalies in our study population substantially varied (central nervous system, face, heart, lung, gastrointestinal, genitourinary, skeletal, and other multiple anomalies; fetal hydrops; and chromosomal or genetic syndromes). However, the numbers of congenital anomalies in each type were too small to analyze the changes in the types of congenital anomaly according to the periods.

We found that the rates of GDM and preeclampsia increased significantly over the study periods. The increasing rates of GDM could be attributed to increased diagnostic sensitivity owing to changes in the GDM diagnostic criteria. In our institution, the diagnostic criteria for GDM were changed from the NDDG criteria to the Carpenter and Coustan criteria in 2005. However, the rate of GDM increased when either criterion was applied. Increased maternal age could be another plausible cause for the increased rates of GDM and preeclampsia. Advanced maternal age is known to be an independent risk factor for various obstetric complications, including preeclampsia, GDM, and preterm birth [17].

The most controversial finding of our study was the change in the preterm birth rates. Twin pregnancies are associated with a high risk for preterm birth [18]. Uterine overdistension and subsequent preterm uterine contractions and preterm labor may be responsible for the high preterm birth risk in twin pregnancies [19]. IIOC is another cause of preterm birth. A recent study found that the incidence of IIOC in twin pregnancies was 7 times greater than that in singleton pregnancies [20]. Increased uterine pressure, greater uterine weight, and increased intra-abdominal pressure have been reported as reasons for the higher risk of IIOC in twin pregnancies [21]. In our study, the rate of IIOC increased over the periods; however, the absolute incidence of IIOC was too low to have an effect on the preterm birth rate in our study population.

In fact, the preterm birth rate decreased significantly over the study periods, mainly owing to the significant decrease in the late preterm twin birth rate, despite an increase in the early preterm birth rate. The optimal gestational age for the delivery of twin pregnancies has been a controversial issue. At our institution, elective cesarean delivery of twin pregnancies was commonly performed at 34–36 weeks before the mid-2000s owing to the misconception that twins matured earlier than did singletons; therefore, gestational ages of 34–36 weeks could be regarded as a term age for twin pregnancies. However, after the mid-2000s, the issue of late preterm, as well as the optimal gestational age of delivery for twin pregnancies, has drawn increasing attention. According to population-based studies, the neonatal mortality rate of twin pregnancy was the lowest between 37 and 39 weeks of gestation [22,23], although the optimal gestational age at delivery is considered to be different for monochorionic and dichorionic twin pregnancies [24,25]. Vergani et al. [26] reported that the rates of stillbirth and perinatal mortality were the lowest in neonates born later than 36 weeks and 37 weeks of gestation in monochorionic and dichorionic twins, respectively. Newman and Unal [27] recommended delivery of dichorionic and monochorionic twins at gestational age 38 weeks and between 34 and 37 weeks, respectively. The National Institutes of Health and Society for Maternal-Fetal Medicine workshop recommended an optimal gestational age for the delivery of monochorionic and dichorionic twins of 34–37 and 38 weeks, respectively [28]. The United Kingdom National Institute for Health and Clinical Excellence Guidelines recommended that women with uncomplicated monochorionic and dichorionic twin pregnancies should deliver electively after 36 and 37 weeks, respectively [29]. Recently, we investigated the maternal and neonatal outcomes of uncomplicated twin pregnancies and found that the optimal gestational age of delivery for uncomplicated monochorionic and dichorionic twin pregnancies was ≥36 and ≥37 weeks, respectively [30]. These study results and guidelines influenced the practice patterns of our institution, decreasing the rate of elective late preterm gestation deliveries performed.

The decrease in the late preterm birth rate was associated with the decreased rates of NICU admission and neonates with low Apgar scores. Recently, we reported that late preterm twin infants had higher risks of adverse neonatal outcomes, such as NICU admission and requirement for mechanical ventilator support [31]. In contrast, the increases in the NICU stay duration, rate of ventilator treatment, duration of assisted ventilation, and rate of RDS might be associated with the increased rate of early preterm birth because these complications mainly occur in neonates born at early preterm gestation [32].

The mode of delivery in the twin pregnancies also changed significantly in our study population during the 24-year study period. Although the vaginal delivery rate increased significantly over the study period, from only 2.2% in period 1 to 10.8% in period 4, the majority of the twins at our institution were delivered via cesarean section. The high cesarean section rate may be associated with the high rates of obstetrical complications, such as preterm birth, GDM, gestational hypertension, fetal anomalies, and fetal growth restriction, at our tertiary referral hospital. However, a more probable reason was that both pregnant women and obstetricians preferred cesarean sections as a safer method of delivery for twins. In some studies, cesarean delivery reduced the risk of adverse neonatal outcomes of twins [33,34]; however, a recent multicenter, randomized controlled trial [35] and systematic reviews [36-38] reported that the delivery mode was not associated with adverse neonatal outcomes in twin pregnancies. Furthermore, the number of pregnant women and obstetricians who prefer vaginal delivery has been increasing, especially when both twins have cephalic presentations.

The strength of our study was that it had a large sample size of 2,133 twin pregnancies. However, this study was limited by the disadvantages inherent in a retrospective study design, which include information bias and misclassification bias. Moreover, the guidelines and protocols in obstetrics and neonatology might not have been consistent over the study period. For example, the reference curves for the birth weight percentiles used in our NICU had been changed during the study period. Since 2015, new reference curves based on the data from the Korean Statistical Information Service published in 2014 have been used [39]. The sudden increase in the rate of SGA in period 4 (2013–2018) might be attributed to this change. Another limitation was that the cut-off for SGA (<10th percentile for gestational age) for twins was defined by the reference curves of singletons because we did not have reference curves for twins. In addition, the study findings have limited generalizability because the study population was from a single center.

In conclusion, this study found that the rates of twin pregnancies have increased steadily over the last 24 years at our institution, and this increase was attributed to advanced maternal age and increased use of ART. Maternal age and the incidence of obstetric complications, such as congenital fetal anomalies, IIOC, preeclampsia, and GDM, increased over the study periods. The increase in the rates of early preterm births was associated with the increases in the rates of RDS and duration of ventilator use. In contrast, the decrease in the rate of NICU admission was associated with the decreased rate of late preterm births, especially elective late preterm births. Further studies are needed to determine a management strategy to minimize maternal obstetric complications and improve neonatal outcomes in twin pregnancies.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Ethical approval

This study was approved by our Institutional Review Board for Clinical Research in Samsung Medical Center (SMC 2015-10-179).

Patient consent

Informed consent was waived because of the retrospective study design.

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