A Specialised Twin Pregnancy Clinic in a Public Hospital

WK YUNG MBBS, MRCOG, FHKAM (O&G)
AL LIU MBBS, MRCOG
SF LAI MBBS
MT LAM MBBS
HN YEUNG MBBS, MRCOG, FHKAM (O&G)
FK LAI BSc (N), MSSc
TK LO MBBS, MRCOG, FHKAM (O&G)
WL LAU MBBS, FRCOG, FHKAM (O&G)
WC LEUNG MBBS, MD, FRCOG, FHKAM (O&G), Cert RCOG (Maternal and Fetal Med)
Department of Obstetrics and Gynaecology, Kwong Wah Hospital, 25 Waterloo Road, Kowloon, Hong Kong

Objectives: To evaluate the pregnancy outcomes in a 3-year cohort of twin pregnancies managed in a specialised clinic, and propose performance indicators for such a 'twin clinic'.
Methods: Prospective data analysis was performed on all the twin pregnancies referred to the twin clinic in Kwong Wah Hospital from 1 April 2006 to 31 March 2009. The specialist clinic and delivery protocol was described. A total of 215 twin pregnancies were identified from the booking system; 207 records were reviewed. Of these, 136 dichorionic diamniotic and 68 monochorionic diamniotic pregnancies were analysed for their characteristics, complications, and maternal and neonatal outcomes. Multivariate analysis was used to identify the risk factors for adverse neonatal outcomes.
Results: Apart from twin-twin transfusion syndrome, chorionicity did not account for differences in pregnancy characteristics, pregnancy complications, and maternal, fetal or neonatal outcomes. Growth discordance greater than 25% on antenatal ultrasound predicted neonatal intensive care unit admission (11.7% vs. 47.5%; p=0.011), composite neonatal morbidity (36.9% vs. 65.0%; p=0.010), low birth weight corrected for gestation (25.8% vs. 45.0%; p=0.001), and prematurity before 37 weeks of gestation (40.3% vs. 65.0%; p=0.006), 34 weeks of gestation (8.1% vs. 30.0%; p=0.003) and 32 weeks of gestation (2.7% vs. 15.0%; p=0.022). Small-for-gestational age on antenatal ultrasound only predicted neonatal intensive care unit admission (13.2% vs. 29.8%; p=0.028). Further analysis on actual birth weight discordance greater than 25% and low birth weight after delivery reinforced its correlation with adverse neonatal outcomes. In Kwong Wah Hospital, sonographic prediction of birth weight discordance greater than 25% had a sensitivity of 73.3%, specificity of 94.1%, positive predictive value of 55.0%, and negative predictive value of 97.3%.
Conclusion: Birth weight discordance and low birth weight are the established risk factors of neonatal morbidity and mortality. As these two parameters could be predicted with reasonable accuracy by means of antenatal ultrasound, we propose 'prediction of birth weight discordance or low birth weight by antenatal ultrasound with positive correlation to adverse neonatal outcomes' to be the potential performance indicator for a specialised clinic managing twin pregnancies.
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Introduction

Although multiple pregnancies only account for 1 to 3% of all live births, they are responsible for a disproportionate share of the maternal-fetal morbidity and mortality[1,2]. The worldwide incidence of multiple pregnancy has risen in recent decades, largely because of assisted reproduction.

In the last decade, antenatal care tends to be sub-specialised and multi-disciplinary. Advocates believe that the specialist clinic model allows doctors and midwives interested in the field to provide antenatal care tailored to individuals. Concentration of expertise and the use of protocols could provide a more focused and consistent care, beneficial to both the service and training. Knox and Martin[3] summarised the potential advantages of specialist clinics for multiple pregnancy as follows:

- Specialist clinics allow earlier identification of complications as there are frequent visits to staff, who are 'tuned' and more 'experienced'. With

Correspondence to: Dr WK Yung
Email: cherrieyung@gmail.com

appropriate monitoring and timing of delivery, pregnancy outcome may be improved.

- Specialist clinics enhance training, allowing more time and resources to teach doctors, midwives and medical students, as the cohort of patients present frequently and consistently; therefore continuity of care is possible.
- Research and audit is easier as centralisation of care aids in development of a database.
- Patients tend to appreciate specialist clinics, as they are usually less overcrowded and the waiting time is shorter. Antenatal care is more individualised and patients usually attain better rapport with the team.

To date there has been no randomised controlled trial to support the role of specialist clinics for multiple pregnancies to improve maternal and baby outcomes[1]. Although some institutions might have their standalone 'multiple pregnancy clinic', there are few publications on their antenatal care and pregnancy outcome.

The Specialist Clinic and Delivery Protocol

The structure of maternity services varies in different places. In Hong Kong, there are two settings; one is a public service provided by the Hospital Authority which is a government-funded body, and the other is private service in which expenses are shared by patients and their insurance cover (if any).

Kwong Wah Hospital (KWH) is one of the eight public hospitals in the territory providing obstetric services that deal with almost 6000 deliveries annually. Patients received obstetric care at minimal personal cost as the service is largely funded by the government. Obstetricians and midwives are salaried and their advice is therefore not influenced by personal financial gain. In public hospitals, delivery is conducted by the on-call team of obstetricians and midwives rather than the clinicians responsible for antenatal care. Some local women receive antenatal service under both public and private systems, as shared care is allowed.

In April 2000, a multiple pregnancy clinic was established in KWH to enhance clinical care and promote research. This specialist clinic was located at the day assessment centre. The team consisted of obstetricians sub-specialised in maternal-fetal medicine, general obstetricians working under supervision, and nurse specialists and midwives interested in the field. Ultrasound assessment was available on site for all women at every antenatal visit. Scanning was performed by the obstetrician who offered counselling and management at the same visit, according to the condition of the pregnancy. Management tended to be centralised with the aim of preventing treatment delay and care fragmentation. There was a department protocol on management of multiple pregnancies that was last updated in 2007. As triplet or higher-order pregnancies are less common, the focus of discussion in this article is mainly on twin pregnancies.

Diagnosis of twin pregnancy was usually made at the general antenatal clinic. A dating scan and determination of chorionicity was performed by specially trained midwives or obstetricians. The women were then referred to the twin clinic for subsequent follow-up. Screening for Down's syndrome was offered to women of or greater than 35 years old at the expected date of confinement. A detailed structural scan was performed at 18 to 22 weeks' gestation. The timing of the visit was largely determined by chorionicity. Monochorionic twins were seen every 2 to 3 weeks from 14 weeks of gestation to look for signs of twin-twin transfusion syndrome (TTTS). Dichorionic twins were scanned every 4 weeks; if suboptimal growth or growth discordance was noticed, more frequent scans were offered. Timing and mode of delivery was discussed and reviewed throughout the pregnancy. Uncomplicated monochorionic diamniotic (MCDA) or dichorionic diamniotic (DCDA) twins were usually delivered at 38 weeks' gestation. For monochorionic monoamniotic (MCMA) twins, prophylactic steroids were given at 32 weeks' gestation and delivery was considered after 32 weeks' gestation. If vaginal delivery was contemplated, labour was closely monitored. Delivery of a twin pregnancy was conducted by obstetricians (in the presence of a senior with more than 4 years' experience in obstetrics). All elective and emergency Caesarean sections were carried out in the operating theatre within the delivery suite with senior obstetricians present. Paediatricians were present at all the deliveries, regardless of gestation.

This study aimed to evaluate the maternal and neonatal outcomes of a 3-year cohort of twin pregnancies managed in the specialist clinic, with a view to proposing performance indicators for the 'twin clinic'.

Methods

A prospective data analysis was performed on all twin pregnancies referred to the Twin Clinic in KWH from 1 April 2006 to 31 March 2009. All antenatal and peripartum events, as well as maternal and neonatal outcomes of the cohort, were followed through. Women with higher-order pregnancies after fetal reduction or spontaneous fetal demise resulting in twin pregnancies were also included.

The women were identified from the Twin Clinic's booking system. Antenatal outpatient and inpatient records, discharge summaries, ultrasound reports, blood test reports, pathology reports, delivery records, and operation records were all traced. The electronic patient record system also allowed retrieval of medical notes of the mothers who delivered in the other public hospitals. Information was identified regarding maternal age, education level, previous obstetric history, mode and place of conception, chorionicity of pregnancy, pre-pregnancy body mass index (BMI) and weight gain, pre-defined antenatal complications, steroid administration, mode of delivery and its indications, pre-defined intrapartum and postpartum complications, and length of postnatal stay. The neonatal records were traced for information on Apgar scores, birth weight, cord blood pH, newborn resuscitation, admission to the neonatal intensive care unit (NICU) and the length of stay, and any pre-defined morbidities and mortality.

Pre-specified definitions were used during the review of maternal and fetal complications.

For maternal complications, hyperemesis was defined as vomiting for which the patient was hospitalised. Anaemia was defined as a haemoglobin level below 100 g/l. Gestational impaired glucose tolerance or diabetes was diagnosed by the 75 g oral glucose tolerance test using World Health Organization criteria. Gestational hypertension was defined as a persistently high systolic blood pressure (BP) [≥140 mm Hg] or diastolic BP (≥90 mm Hg). Gestational proteinuria was defined as proteinuria ≥300 mg/24 hours. Pre-eclampsia was defined according to internationally established criteria. Preterm labour was defined as regular uterine contractions leading to progressive dilatation of the cervix at <37 weeks' gestation. Preterm pre-labour rupture of membrane was defined as rupture of membranes before onset of labour at <37 weeks' gestation. Antepartum haemorrhage was defined as any bleeding from the genital tract after 24 weeks of gestation.

For fetal complications, miscarriage was defined as spontaneous loss of a pregnancy before 24 weeks of gestation. Single fetal demise was defined as loss of one fetus after 12 weeks of gestation. TTTS was staged using the Quintero classification system. Fetal structural abnormalities were divided into major and minor. Small-for-gestational age (SGA) was defined as estimated fetal weight <10th centile on the scan prior to delivery; large-for-gestational age was defined as ≥90th centile on the scan prior to delivery. Discordant growth was defined as intra-pair difference in estimated fetal weight on ultrasound of >25%.

For intrapartum and postpartum events, a febrile condition was defined as persistent increase in oral temperature to ≥37.4°C and recourse to antibiotic treatment. Adherent placenta was defined as difficulty in delivering the whole or part of the placenta. Secondary postpartum haemorrhage was recorded if the patient was readmitted after the postnatal discharge with concern about abnormal vaginal bleeding within 6 weeks of delivery.

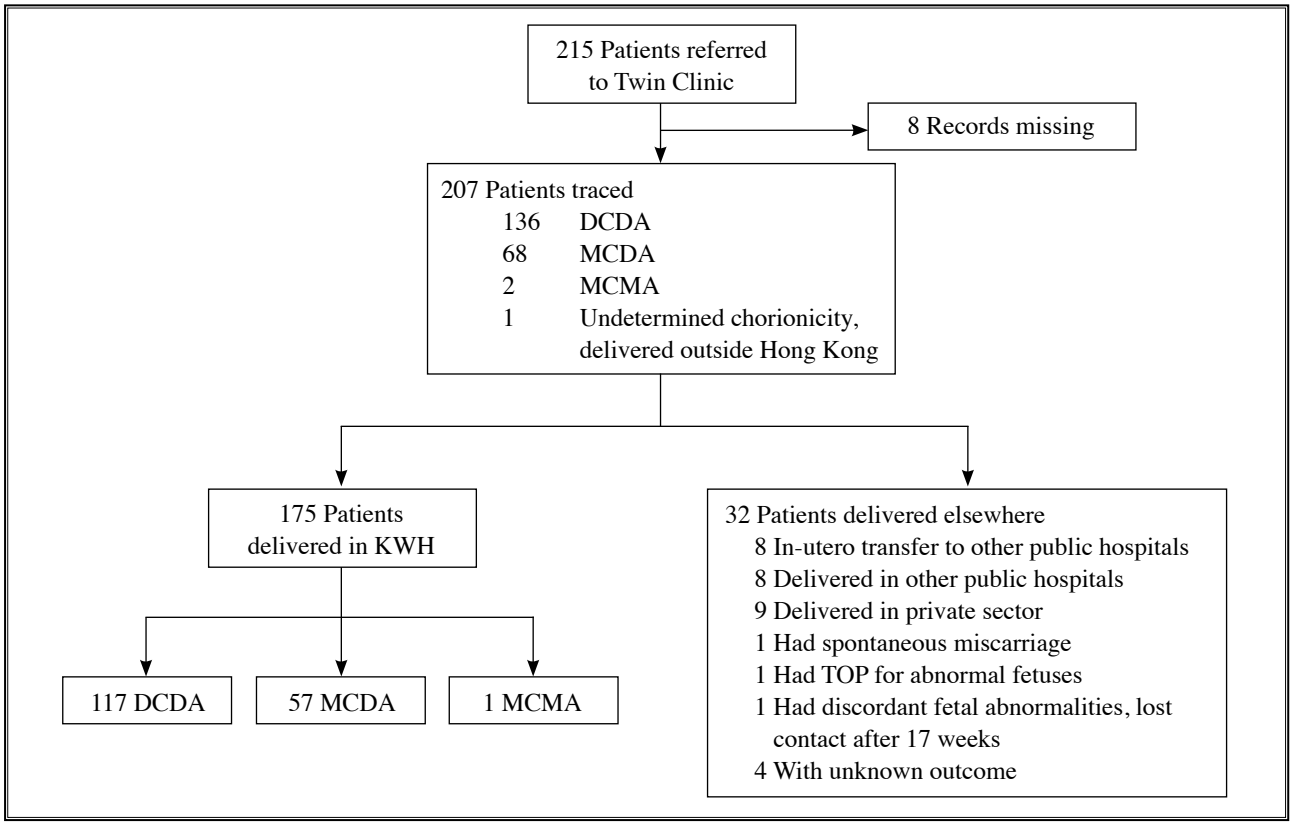
For neonatal morbidities, low birth weight was defined as a birth weight <10th centile adjusted for gestation. Neonatal jaundice was recorded as complication only if phototherapy was offered. Hypoglycaemia was defined by a serum glucose <2.6 mmol/l. Respiratory distress syndrome was a clinical diagnosis with radiological support. Transient tachypnoea of the newborn was a self-limiting respiratory disorder, without evidence of respiratory distress syndrome on X-ray. Sepsis was diagnosed either with positive culture or clinically with evidence from serum markers. Necrotising enterocolitis was diagnosed by the neonatologist with radiological support. Intraventricular haemorrhage referred to bleeding within the ventricle with or without ventricular dilatation. A cephalohaematoma was a subperiosteal collection of blood based on a clinical diagnosis. Apnoea of prematurity was a clinical diagnosis according to established criteria.

All the information was manually reviewed and entered into a database using SPSS (Windows version 16.0) for statistical analysis. Maternal and neonatal outcomes were presented according to their chorionicity. Analysis of risk factors for perinatal outcome variables was performed by logistic regression. Differences within each category were determined with statistical significance calculated by chi-square test. A p value of <0.05 was considered significant. Ethics approval was obtained from the hospital ethics committee.

Results

This prospective review involved 215 twin pregnancies booked in the twin clinic from 1 April 2006 to 31 March 2009 (3 years). A total of 207 records were reviewed as eight records were reported 'missing'. Figure 1 shows the flowchart of the 215 women who made a booking in the Twin Clinic in the pre-defined period. Table 1 shows the demographic characteristics of the 207 women.

Chorionicity was prospectively determined in 196 (94.7%) of the pregnancies with 98% accuracy confirmed by histopathological examination of placenta. Chorionicity was not determined in 11 pregnancies because of late



Abbreviations: DCDA = dichorionic diamniotic; MCDA = monochorionic diamniotic; MCMA = monochorionic monoamniotic; KWH = Kwong Wah Hospital; TOP = termination of pregnancy

Figure 1. Flowchart of women booked in Twin Clinic

booking. They were all managed according to the protocol for monochorionic twins. Women were allocated to their respective group for analysis according to the chorionicity by placental histopathology if it was available. One patient was delivered outside Hong Kong at 25 weeks of gestation, with unknown chorionicity. This case was excluded from analysis.

There were two (1.0%) MCMA twin pregnancies in the cohort. One woman was lost to contact after 20 weeks' gestation. The other delivered at 33 weeks' gestation by elective lower segment Caesarean section (LSCS) according to protocol. Both babies were born in good condition. They were admitted to NICU for 8 and 18 days, respectively because of respiratory distress syndrome and neonatal jaundice. Because of its rarity, the two MCMA pregnancies were excluded from analysis.

The pregnancy characteristics of the remaining 204 pregnancies are shown in Table 2. Among these, 174 (85%) of the women delivered 345 livebirths in KWH and were entered into the full analysis. The peripartum events of the 174 women are shown in Table 3.

There were two cases of TTTS. Both were referred to a tertiary centre for fetoscopic laser therapy. One

Table 1. Demographics of the 207 women

Demographics	Data*
Age (years)	31.6 ± 4.0
<35	165 (79.7)
≥35	42 (20.3)
Parity	
Nulliparous	153 (73.9)
Mode of conception	
Spontaneous	123 (59.4)
Assisted (IVF)	50 (24.2)
Assisted (non-IVF)	34 (16.4)
Marital status	
Married	206 (99.5)
Education level	
Primary	6 (2.9)
Secondary	118 (57.0)
Tertiary	79 (38.2)
Unknown	4 (1.9)
Smoking	18 (8.7)
Alcohol use	3 (1.4)
Recreational drug use	0
Family history of multiple pregnancy	31 (15.0)

Abbreviation: IVF = in-vitro fertilisation

* Data are given as No. (%) or mean ± standard deviation

pregnancy resulted in fetal demise of the 'donor' twin 1 day after procedure. The 'recipient' twin was delivered (in good condition) at 37 weeks' gestation. The other pregnancy was not delivered in KWH.

There were four pregnancies with a single intrauterine fetal demise (IUFD) in the cohort. One was the victim of TTTS as mentioned before. The second one was the victim of selective intrauterine growth restriction (sIUGR) in an MCDA twin pregnancy. Discordant growth was noticed at 25 weeks' gestation and the smaller fetus died 1 week after the diagnosis. The surviving fetus was delivered at 36 weeks of gestation with low birth weight. The third IUFD occurred on an MCDA twin pregnancy at 17 weeks of gestation, with no evidence of TTTS or sIUGR. The surviving fetus was delivered spontaneously in good condition, at 37 weeks of gestation. The last IUFD occurred on a DCDA twin pregnancy at 12 weeks of gestation. The surviving fetus was delivered in good condition, at 37 weeks of gestation.

There were two women who suffered massive postpartum haemorrhage (blood loss >2000 ml). The first one was a DCDA twin pregnancy delivered by elective LSCS at 38 weeks of gestation at the patient's request. It was complicated by uterine atony and eventually a hysterectomy was performed. The second case was a DCDA twin pregnancy with a uterine fibroid. Emergency LSCS was performed for poor progress of labour. There was heavy bleeding from the placental bed, which was controlled by haemostatic stitches.

Three women were admitted to the intensive care unit in the postpartum period. There was no maternal mortality. Neonatal outcomes of the 345 babies born to these mothers in KWH are shown in Table 4. There was one case of birth trauma; a fractured femur of the first twin (delivered by elective LSCS). There was no neonatal mortality in the cohort.

For the prediction of adverse neonatal outcome, chorionicity was only associated with the number of days stayed in NICU (MCDA vs. DCDA; 16 ± 13 vs. 11 ± 10; p=0.024) and hypoglycaemia (MCDA vs. DCDA; 18.0%

Table 2. Pregnancy characteristics of the 204 DCDA and MCDA twin pregnancies

Characteristic	DCDA* (n = 136)	MCDA* (n = 68)	p Value
Mean gestation at booking (weeks)	14.5 ± 4.2	14.4 ± 3.5	0.792
Dating scan	130 (95.6)	66 (97.1)	0.610
Down's screening for age ≥35 years	20 (76.9)	13 (81.2)	0.769
Scanning of cervical length	48 (35.3)	28 (41.2)	0.413
BMI (kg/m^2)	20.8 ± 2.3	20.7 ± 2.6	0.614
Hyperemesis need admission	2 (1.5)	0	0.318
Anaemia	19 (14.0)	11 (16.2)	0.875
IGT/GDM	34 (25.0)	21 (30.9)	0.405
Gestational proteinuria	3 (2.2)	4 (5.9)	0.225
Pre-eclampsia / HELLP	10 (7.4)	4 (5.9)	0.954
Antepartum haemorrhage	13 (9.6)	3 (4.4)	0.288
Threatened preterm labour <34 weeks	20 (14.7)	12 (17.6)	0.434
Miscarriage	1 (0.7)	0	0.485
Single fetal demise	1 (0.7)	3 (4.4)	0.766
Fetal reduction	4 (2.9)	0	-
Abnormal fetal structures (major)	1 (0.7)	3 (4.4)	0.462
TTTS	0	2 (2.9)	0.042
Discordant growth >25% on USG	14 (10.3)	7 (10.3)	0.824
SGA on USG (one or both fetuses)	32 (23.5)	12 (17.6)	0.450
Antenatal corticosteroid	33 (24.3)	15 (22.1)	0.890

Abbreviations: DCDA = dichorionic diamniotic; MCDA = monochorionic diamniotic; BMI = body mass index; IGT/GDM = impaired glucose tolerance/gestational diabetes mellitus; HELLP = haemolysis, elevated liver enzymes, low platelets; TTTS = twin-twin transfusion syndrome; USG = ultrasonography; SGA = small-for-gestational age

* Data are given as No. (%) or mean ± standard deviation

Table 3. Peripartum events of 174 pregnancies delivered in Kwong Wah Hospital

Peripartum event	DCDA* (n = 117)	MCDA* (n = 57)	p Value
Gestation at delivery (weeks)	36.3 ± 1.88	36.1 ± 1.99	0.099
Preterm delivery (weeks)			
<37	72 (61.5)	29 (50.9)	0.181
<34	11 (9.4)	6 (10.5)	0.815
<32	3 (2.6)	4 (7.0)	0.161
<30	1 (0.9)	0	0.484
Mode of delivery (twin I)			
Vaginal delivery	14 (12.0)	15 (26.3)	0.042
Emergency Caesarean section	46 (39.3)	22 (38.6)	
Planned elective Caesarean section	57 (48.7)	20 (35.1)	
Intrapartum complication			
IP PET/ eclampsia	6 (5.1)	2 (3.5)	0.981
Twin 1 fetal distress	1 (0.9)	3 (5.3)	0.077
Twin 2 fetal distress	2 (1.7)	1 (1.8)	0.989
Placenta abruption	4 (3.4)	1 (1.8)	0.511
Cord prolapse	2 (1.7)	2 (3.5)	0.046
IP febrile condition	2 (1.7)	2 (3.5)	3.978
Adherent placenta	0	2 (3.5)	-
Blood loss ≥1000 ml	10 (8.5)	4 (7.0)	0.533
Blood transfusion	7 (6.0)	4 (7.0)	0.752
Compression suture	3 (2.6)	0	0.704
Hysterectomy	1 (0.9)	0	0.473
Admission to ICU	2 (1.7)	1 (1.8)	1.000
Postpartum complication			
Febrile condition or wound infection	5 (4.3)	3 (5.3)	0.718
RPOG	0	4 (7.0)	0.004
Wound haematoma	1 (0.9)	0	0.476
Secondary PPH	1 (0.9)	2 (3.5)	0.807
PET	3 (2.6)	2 (3.5)	0.097
Others	1 (0.9)	0	0.476

Abbreviations: DCDA = dichorionic diamniotic; MCDA = monochorionic diamniotic; IP = intrapartum; PET = pre-eclampsia; ICU = intensive care unit; RPOG = retained products of gestation; PPH = postpartum haemorrhage

* Data are given as No. (%) or mean ± standard deviation

vs. 9.4%; p=0.033). Other potential predictive factors, including maternal age, parity, BMI, method of conception, pregnancy complications, ultrasound measurement of fetal size and growth discordance, and mode of delivery were analysed further. We found that if the intra-pair growth discordance was >25% on ultrasound, it was associated with higher rate of NICU admission (11.7% vs. 47.5%; p=0.011) and composite neonatal morbidity (36.9% vs. 65.0%; p=0.010). The difference remained significant under logistic regression adjusted for influences from prematurity (<34 weeks of gestation), SGA, chorionicity, mode of delivery, maternal demographics and pregnancy complications. Discordant growth of >25% was also associated with a higher risk of prematurity, namely: <37 weeks of gestation (40.3% vs. 65.0%; p=0.006), <34 weeks of gestation (8.1% vs. 30.0%, p=0.003) and <32 weeks of gestation (2.7% vs. 15.0%, p=0.022). This finding remained significant following logistic regression adjusted for influences from chorionicity, maternal demographics, and pregnancy complications. However, if iatrogenic deliveries were excluded from analysis, the association between intra-pair discordant growth and prematurity was no longer valid. The results are presented in Table 5.

Table 4. Neonatal outcome of 345 babies born in Kwong Wah Hospital

	DCDA* (n = 234)	MCDA* (n = 111)	p Value
Birth weight (kg)	2.3 ± 0.5	2.3 ± 0.6	0.428
Low birth weight <10th centile	67 (28.6)	29 (26.1)	0.516
High birth weight >90th centile	0	1 (0.9)	0.157
Low AS			
AS (1) <7	9 (3.8)	3 (2.7)	0.907
AS (5) <7	2 (0.9)	0	0.329
Cord blood pH <7.20	10 (4.3)	10 (9.0)	0.704
Newborn resuscitation	5 (2.1)	1 (0.9)	0.412
NICU admission	35 (15.0)	18 (16.2)	0.762
No. of days in NICU	11 ± 10	16 ± 13	0.024
Neonatal morbidity			
Neonatal jaundice	23 (9.8)	10 (9.0)	1.000
Hypoglycaemia	22 (9.4)	20 (18.0)	0.033
Respiratory distress syndrome	19 (8.1)	10 (9.0)	0.836
TTTN	9 (3.8)	3 (2.7)	0.758
Clinical sepsis	14 (6.0)	6 (5.4)	1.000
Apnoea of prematurity	5 (2.1)	3 (2.7)	0.716
Necrotising enterocolitis	5 (2.1)	0	0.180
Electrolyte disturbance	3 (1.3)	2 (1.8)	0.658
Blood transfusion	3 (1.3)	0	0.554
Cephalohaematoma	1 (0.4)	1 (0.9)	0.541
Intraventricular haemorrhage	0	1 (0.9)	0.322
Hypothyroidism	2 (0.9)	0	1.000
Skin cellulitis	2 (0.9)	0	1.000
Pneumothorax	1 (0.4)	0	1.000
Birth trauma (fractured femur)	1 (0.4)	0	1.000
Major congenital abnormalities			
Heart disease (no heart failure)	7 (3.0)	6 (5.4)	0.363
Heart disease (with heart failure)	2 (0.9)	2 (1.8)	0.597
Syndromal disorder	2 (0.9)	0	1.000
Pneumomediastinal tumour	1 (0.4)	0	1.000
Prominent ventricle	1 (0.4)	0	1.000
Minor congenital abnormalities	8 (3.4)	7 (6.3)	0.260

Abbreviations: DCDA = dichorionic diamniotic; MCDA = monochorionic diamniotic; AS = Apgar score; NICU = neonatal intensive care; TTTN = transient tachypnoea of newborn

* Data are given as No. (%) or mean ± standard deviation

Based on a similar logistic regression analysis for SGA, we found that an estimated fetal weight of <10th centile on ultrasound could predict NICU admission (13.2% vs. 29.8%; p=0.028) but not neonatal morbidity or prematurity. The results are shown in Table 6.

Discordant growth on ultrasound also predicted low birth weight (25.8% vs. 45.0%; p=0.001) as shown in Table 5. This finding was valid after excluding influences from chorionicity, maternal demographics, and pregnancy complications by logistic regression.

Combining the two risk factors was a strong predictor of NICU admission. This was exemplified by SGA combining with: significant (>25%) growth discordance (13.8% vs. 58.8%, p=0.001), composite neonatal morbidity (38.2% vs. 82.4%; p=0.002), prematurity before 34 weeks (9.2% vs. 35.3%; p=0.002) and before 32 weeks of gestation

Table 5. Discordant growth on ultrasound in relation to neonatal outcome and prematurity

	% Growth discordance on ultrasound*		p Value	OR	CI
	≤25% (n = 298)	>25% (n = 40)			
Neonatal resuscitation	4 (1.3)	2 (5.0)	0.929	2.228E14	-
NICU admission	35 (11.7)	19 (47.5)	0.011	8.038	1.628-39.691
Composite neonatal morbidity	110 (36.9)	26 (65.0)	0.010	3.440	1.338-8.849
AS (1) <7	10 (3.4)	2 (5.0)	0.855	0.569	0.077-4.091
AS (5) <7	2 (0.7)	0	1.00	-	-
Cord blood pH < 7.20	17 (5.7)	2 (5.0)	0.276	2.994	0.417-21.526
Low birth weight <10th centile	77 (25.8)	18 (45.0)	0.001	3.553	1.644-7.681
Prematurity (weeks)					
<37	120 (40.3)	26 (65.0)	0.006	3.186	1.398-7.257
<34	24 (8.1)	12 (30.0)	0.003	4.575	1.671-12.528
<32	8 (2.7)	6 (15.0)	0.022	6.846	1.324-35.402
<30	2 (0.7)	0	0.997	-	-
Non-iatrogenic prematurity (weeks)					
<37	116 (38.9)	16 (40.0)	0.780	1.121	0.503-2.496
<34	24 (8.1)	8 (20.0)	0.232	1.966	0.649-5.956
<32	8 (2.7)	4 (10.0)	0.312	2.626	0.404-17.087

Abbreviations: OR = odds ratio; CI = confidence interval; NICU = neonatal intensive care unit; AS = Apgar score
* Data are given as No. (%)

Table 6. Small-for-gestational age on ultrasound in relation to neonatal outcome and prematurity

	Estimated fetal weight by ultrasound*		p Value	OR	CI
	≥10th centile (n = 295)	<10th centile (n = 47)			
Neonatal resuscitation	3 (1.0)	1 (2.1)	0.922	4.272E8	-
NICU admission	39 (13.2)	14 (29.8)	0.028	5.973	1.215-29.373
Composite neonatal morbidity	112 (38.0)	25 (53.2)	0.221	1.663	0.736-3.758
AS (1) <7	10 (3.4)	2 (4.3)	0.737	0.665	0.098-4.396
AS (5) <7	2 (0.7)	0	1.000	-	-
Cord blood pH <7.20	18 (6.1)	1 (2.1)	0.615	0.550	0.053-5.664
Preterm delivery (weeks)					
<37	125 (42.4)	20 (42.6)	0.637	0.838	0.402-1.745
<34	26 (8.8)	8 (17.0)	0.623	1.289	0.468-3.548
<32	9 (3.1)	3 (6.4)	0.783	0.779	0.133-4.582
<30	0	0	1.000	-	-

Abbreviations: OR = odds ratio; CI = confidence interval; NICU = neonatal intensive care unit; AS = Apgar score
* Data are given as No. (%)

(3.4% vs. 17.6%; p=0.017). The difference remained valid after adjustment for influences from chorionicity, maternal demographics, pregnancy complications, and mode of delivery by logistic regression (Table 7).

Tables 8 and 9 show the correlation of actual birth weight discordance and low birth weight with adverse neonatal outcome and prematurity. The findings were coherent with the prediction on antenatal ultrasound. The diagnostic indices of ultrasound prediction on birth weight discordance and low birth weight are shown in Table 10.

Discussion

Twin pregnancy is considered as high risk. The increased maternal risk is well-recognised and reported

Table 7. Discordant growth and SGA on ultrasound in relation to neonatal outcome and prematurity

	% Growth discordance and SGA on ultrasound*		p Value	OR	CI
	≤25% (n = 325)	>25% (n = 17)			
Neonatal resuscitation	5 (1.5)	1 (5.9)	0.982	9.477E9	-
NICU admission	45 (13.8)	10 (58.8)	0.001	20.107	3.869-162.93
Composite neonatal morbidity	124 (38.2)	14 (82.4)	0.002	10.794	2.427-47.999
AS (1) <7	11 (3.4)	1 (5.9)	0.287	0.515	0.025-2.988
AS (5) <7	2 (0.6)	0	1.000	1.826	-
Cord blood pH <7.20	18 (5.5)	1 (5.9)	0.336	3.118	0.308-31.577
Prematurity (weeks)					
<37	136 (41.8)	11 (64.7)	0.066	2.718	0.934-7.904
<34	30 (9.2)	6 (35.3)	0.002	7.419	2.127-25.872
<32	11 (3.4)	3 (17.6)	0.017	7.500	1.430-39.347
Non-iatrogenic prematurity (weeks)					
<37	127 (39.1)	6 (35.3)	0.665	0.789	0.271-2.302
<34	28 (8.6)	4 (23.5)	0.068	3.490	0.913-13.348
<32	10 (3.1)	2 (11.8)	0.166	3.863	0.570-26.163

Abbreviations: SGA = small-for-gestational age; OR = odds ratio; CI = confidence interval; NICU = neonatal intensive care unit; AS = Apgar score

* Data are given as No. (%)

Table 8. Actual birth weight discordance in relation to neonatal outcome and prematurity

	% Actual birth weight discordance*		p Value	OR	CI
	≤25% (n = 312)	>25% (n = 30)			
Neonatal resuscitation	5 (1.6)	1 (3.3)	0.985	5.774E12	-
NICU admission	37 (11.9)	17 (56.7)	0.071	3.968	0.889-17.723
Composite neonatal morbidity	116 (37.2)	24 (80.0)	0.005	4.791	1.590-14.442
AS (1) <7	10 (3.2)	2 (6.7)	0.411	0.417	0.052-3.365
AS (5) <7	2 (0.6)	0	1.000	827.9	-
Cord blood pH <7.20	19 (6.1)	1 (3.3)	0.885	1.185	0.119-11.845
Prematurity (weeks)					
<37	124 (39.7)	22 (73.3)	<0.001	5.109	2.062-12.657
<34	24 (7.7)	12 (40.0)	<0.001	18.624	6.153-57.586
<32	8 (2.6)	6 (20.0)	0.001	28.708	3.741-220.27
<30	2 (0.6)	0	-	-	-
Non-iatrogenic prematurity (weeks)					
<37	120 (38.5)	12 (40.0)	0.806	1.112	0.476-2.597
<34	24 (7.7)	8 (26.7)	<0.001	9.339	2.931-29.759
<32	8 (2.6)	4 (13.3)	0.026	10.978	1.329-90.713

Abbreviations: OR = odds ratio; CI = confidence interval; NICU = neonatal intensive care unit; AS = Apgar score

* Data are given as No. (%)

extensively in publications[4]. Maternal complications in our cohort were inherent based on local[5] and international data[6-8]. In our cohort, major maternal morbidities included primary postpartum haemorrhage >1000 ml (8.0%), secondary postpartum haemorrhage (1.7%), blood transfusion (6.3%), hysterectomy (0.6%), and ICU admission (1.7%). Increased awareness of risk, adherence to management protocol, and justified selection on time and mode of delivery are ways to reduce maternal morbidity and mortality. Although Caesarean section rate (82%) in our cohort was higher

Table 9. Actual low birth weight in relation to neonatal outcome and prematurity

	Actual birth weight corrected to gestation*		p Value	OR	CI
	≥10th centile (n = 248)	<10th centile (n = 97)			
Neonatal resuscitation	3 (1.2)	1 (1.0)	0.526	0.379	0.019-7.598
NICU admission	31 (12.5)	22 (22.7)	0.003	6.439	1.849-22.424
Composite neonatal morbidity	89 (35.9)	50 (51.5)	0.031	1.916	1.063-3.453
AS (1) <7	9 (3.6)	3 (3.1)	0.836	1.172	260-5.281
AS (5) <7	2 (0.8)	0	0.994	8.414E13	-
Cord blood pH <7.20	15 (6.0)	5 (5.2)	0.498	1.559	0.432-5.627
Preterm delivery (weeks)					
<37	108 (43.5)	37 (38.1)	0.104	0.640	0.374-1.096
<34	22 (8.9)	12 (12.4)	0.309	0.623	0.251-1.549
<32	7 (2.8)	5 (5.2)	0.864	0.869	0.174-4.337
<30	0	0	-	-	-

Abbreviations: OR = odds ratio; CI = confidence interval; NICU = neonatal intensive care unit; AS = Apgar score
* Data are given as No. (%)

Table 10. Diagnostic indices of antenatal ultrasound in Kwong Wah Hospital

	Prediction of birth weight discordance	Prediction of low birth weight
Sensitivity	73.3%	41.7%
Specificity	94.1%	97.2%
Positive predictive value	55.0%	85.1%
Negative predictive value	97.3%	81.0%

than the reported 50 to 67% in the literature[4,5], it was still coherent with the overall rate of 79% in the territory[5]. We do not discuss maternal complications further in this report, as its aim was to evaluate the performance of the Twin Clinic in improving neonatal outcome.

Preterm labour, TTTS and intrauterine growth restriction are the major causes of adverse neonatal outcomes in twin pregnancies.

Transvaginal ultrasound measurement of cervical length in late second trimester (using a threshold of 25 mm) has been proven a useful predictor of preterm labour[9]. However, the recent randomised placebo-controlled trial (STOPPIT study[10]) did not show any benefit from vaginal progesterone in the prevention of preterm labour in twin pregnancies. The rate of preterm delivery in our cohort before 34 and 37 weeks of gestation were 10.3% and 42.0%, respectively. The rate was slightly under-estimated because eight pregnancies were transferred to other obstetric units for preterm delivery (due to unavailability of NICU beds) and were therefore not included in the analysis. The preterm delivery rate described by Fox et al[11] was 16% and 53% at 34 and 37 weeks, respectively. Given only 40% of pregnancies in the cohort with cervical length measured and the lack of effective preventive measures, we do not address this issue further here.

Accurate determination of chorionicity is the key to managing twin pregnancy. Monochorionic twin pregnancy requires closer surveillance. Early detection of TTTS allows in-time referral for fetoscopic laser coagulation of vascular anastomoses, which is beneficial in reducing perinatal mortality. The staging system for TTTS has been well-established by Quintero et al[12], and untreated cases carry high mortality (a 37% survival rate was quoted by van Gemert et al[13] in the past decade). We were surmised that there were only two (3%) monochorionic pregnancies suffering from TTTS in our cohort. The frequency was far lower than the 10 to 15% quoted in the literature[14]. Nevertheless, we think under-diagnosis was not likely, as there were only three single fetal demises in the monochorionic group. The low frequency of TTTS could be due to the small sample size. Whether ethnicity has a bearing requires a larger-scale study in this region.

Regardless of chorionicity, assessment of fetal well-being largely relies on antenatal ultrasound. As mentioned before, the advantage of the Twin Clinic was the combination of clinical assessment, ultrasound scanning, counselling and treatment decisions available during a single visit.

The association of intra-pair weight discordance and low birth weight with adverse neonatal outcomes has been well established[15,16]. Discordance of 25% was chosen as the threshold after review of the literature. The rate of significant discordant growth in our cohort was 12%, which is comparable to 8 to 14% reported in literature[17-19]. Timely delivery of any growth-restricted fetus can reduce the risk of intrauterine death. We postulate that correct prediction of discordant growth and low birth weight by antenatal ultrasound is beneficial and can be used as the objective performance indicator in a twin clinic.

There have been few publications on bench marking of antenatal ultrasound in predicting birth weight discordance[20]. The study with the best performance was conducted by Gernt et al[20] and involved 338 pregnancies. It demonstrated a sensitivity of 55%, specificity of 97%, positive predictive value (PPV) of 82% and negative predictive value (NPV) of 91%. Other studies demonstrated similar specificity and NPV but lower sensitivity (23-43%) and PPV (33-75%)[17-19].

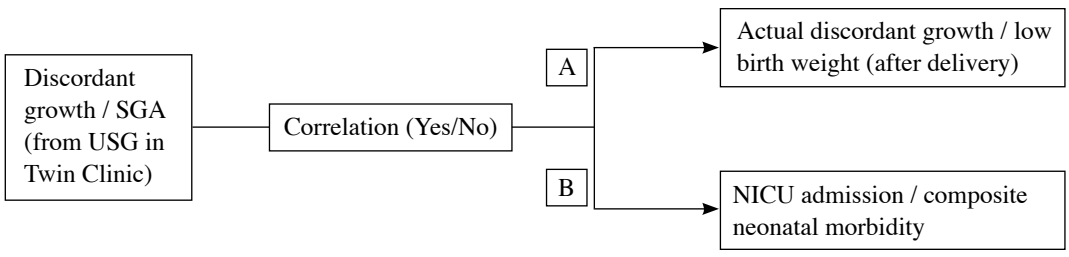
The diagnostic index of our Twin Clinic was comparable to the limited data in literature. The majority of scans were performed by designated obstetricians who were either subspecialist in maternal-fetal medicine or undergoing subspecialist training.

Analysis showed that discordant growth alone or in combination with SGA on ultrasound was a predictor of adverse neonatal outcome, in terms of NICU admission and composite neonatal morbidity. This finding was coherent with the analysis on actual low birth weight and birth weight discordance in relation to adverse neonatal outcome.

We therefore postulate that if ultrasound can correctly predict growth discordance and SGA, such information is beneficial to procuring in-time delivery, which can probably prevent perinatal mortality. On the contrary, incorrect prediction is potentially harmful as unnecessary iatrogenic preterm delivery may increase neonatal morbidity.

In our cohort, antenatal ultrasound assessment of fetal growth was beneficial. Given the high specificity of both parameters, findings of growth discordance or SGA on ultrasound indicated the pregnancy was at risk. This directed the obstetrician to check other parameters, including: liquor volume, umbilical artery and middle cerebral artery Doppler, interval growth and maternal co-morbidities. More frequent follow-up can also be arranged and earlier delivery considered.

One may criticise that our PPV was lower than expected and this might lead to unnecessary intervention. We therefore further analysed the group with iatrogenic delivery before 37 weeks of gestation for fetal well-



Four possible scenarios	A	B	Implications on Twin Clinic performance
1	Yes	Yes	Useful, as USG correctly predicts growth discordance / LBW and this is the proven high-risk group of adverse neonatal outcome
2	Yes	No	Unlikely to happen in real situation as growth discordance and LBW are the established risk factors for adverse neonatal outcome. Advise to evaluate clinical management of newborn or documentation of neonatal outcome
3	No	Yes	Potentially harmful as unnecessary intervention increases neonatal morbidity (i.e. prematurity)
4	No	No	Not useful

Abbreviations: SGA = small-for-gestational age; USG = ultrasonography; NICU = neonatal intensive care unit; LBW = low birth weight

Figure 2. Algorithm to assess the performance of a Twin Clinic

being. Notably, there were 20 pregnancies with significant discordant growth on ultrasound; only eight were delivered preterm by planned induction or Caesarean section. Low birth weight (of one or both fetuses) was correctly predicted in all eight pregnancies, while growth discordance was correctly predicted in seven of them. This implied that (1) the predictive value of ultrasound was still high in the intervention group, and (2) growth discordance or SGA was not the sole indicator to consider early delivery. Other indicators of fetal compromise must have been considered and therefore we did not over-react to these two parameters alone. The NICU admission rate in our cohort was 16%, which was also slightly under-estimated. As mentioned earlier, this was because eight pregnancies were transferred to other obstetric units due to the overloaded NICU. The rate of NICU admission in our territory was 43%[5]; a variable rate of 25 to 50% is quoted in literature[8,21].

Although there is no information from randomised controlled trials to support the role of a 'specialised' clinic over 'standard' antenatal care for twin pregnancies, for decades this has been the practice in many overseas units. Because of the paucity of meaningful research, assessment on performance of such services is difficult. As the first report in the territory on a twin clinic model, we propose 'prediction of birth weight discordance or low birth weight by antenatal ultrasound with positive correlation to adverse neonatal outcome' as a potential performance indicator of the clinic (Figure 2). This parameter is suggested because it can be readily quantified and set as an auditable standard. It should not be taken as the only predictor of adverse neonatal outcomes or the sole indication for interventions.

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