Pregnancy outcomes among 31 patients with tetralogy of Fallot

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Abstract

Background Ttralogy of Fallot (TOF) is a severe type of congenital heart disease (CHD) and confers substantial risk to mother and fetus. However, the outcomes of pregnant women with TOF have not been well studied.

Methods Women with TOF who has been seen and/or delivered at our tertiary-care hospital between April 2008 and January 2018 were retrospective reviewed.

Results A total of 31 TOF patients with pregnancies were identified in ten-year period. Among these patients, cardiac defects were surgically repaired in 19 cases and remained uncorrected in 12 women. The frequency of miscarriages and preterm birth was greater in the uncorrected group (16.67% vs one, and 50% vs 5.26%, respectively). The percentage of babies who were small for gestational age (SGA) was 41.67% and 10.53% in two groups. The neonatal mortality and fetal mortality were observed in women without correction for TOF, which were 3.23% (1/31) and 6.45(2/31), respectively. Maternal and neonatal risk appeared to be associated with heart functional classifications, pulmonary hypertension and histories of cardiac events such as serious cardiac arrhythmias.

Conclusions Obstetric and cardiac complications are more frequently present in the pregnant women with uncorrected TOF. Surgical correction is associated with improved maternal and perinatal outcome.

Introduction

Tetralogy of Fallot (TOF) is a s type of congenital heart disease (CHD) with an incidence of 10% of all reported congenital heart diseases, which is characterized by four components: large ventricular septal defect (VSD), overriding aorta, right ventricular hypertrophy, and right ventricular outflow tract obstruction[1]. In the past decades, the overall prognosis of CHD patient has been greatly improved and many patients could reach adulthood owing to early diagnosis and timely therapy. However, TOF as a serious complex and cyanotic CHD, the prognosis for TOF patients remain poor, especially in those who do not undergo surgical repair.

After corrective surgery, the majority of young women with TOF survive into their reproductive age. Without repair of defects, TOF patients rarely reach childbearing age and get pregnant. Since pregnancy introduces extra load on the heart, and can damage cardiac functions, resulting in the increase in both maternal and perinatal morbidity[2,3].Previous studies have demonstrated that cardiac and obstetric complications are more likely to occur in patients with uncorrected lesions[4–6]. The most common cardiac complications include progressive dilatation of the right ventricle and ventricular failure, thromboembolism, atrial and ventricular arrhythmias, progressive aortic root dilatation and endocarditis[1,7]. The most common obstetric complications include increased risk in miscarriage, premature birth, and low birth weights, postpartum hemorrhage, paradoxical embolism, thromboembolism, congestive cardiac failure, infective endocarditis, and arrhythmias[4]. The pulmonary haemorrhage, brain abscess and thromboembolic complications have been thought to be the most common causes of death[1,8].

To the date, the outcomes of pregnant women with TOF are not well studied due to limited number of cases and lack of data for close follow up. Therefore, the management of TOF pregnant women remains challenging. Here, we present 31 cases of pregnant women with corrected or uncorrected TOF.

Methods

This was a retrospective case series study, which is approved by the Institutional Review Board of West China Second Univery Hospital. Between April 2008 and January 2018, a total of 85184 pregnant women have been seen and gave birth in West China Second University Hospital. A total of 31 pregnant women with TOF were identified and further reviewed and analyzed. We firstly compared the overall clinical characteristics, cardiac and obstetric complications, outcome of pregnancy complications between corrected and uncorrected groups, and then we further analyzed the maternal hemodynamic features and obstetric outcomes in those with uncorrected TOF.

All pregnant women both corrected or not, were evaluated by echocardiography, electrocardiography (ECG), and clinical examinations such as blood pressure (BP), heart rate (HR) etc. Hypertension, diabetes mellitus, and other pregnancy associated diseases were taken into consideration in the clinical characterization of the patients.

Echocardiography

During the past ten years echocardiography as a reliable technique for the detection of CHD and the assessement of haemodynamic status has been very mature. TOF is characterized by VSD with an overriding aorta and anterior deviation of the outlet septum, creating pulmonary stenosis and resulting in right ventricular hypertrophy[1]. The diagnosis of tetralogy of Fallot by echocardiography is based on demonstration of a ventricular septal defect and a large overriding aorta. The ultrasound information concerned valvar function, right ventricular pressure, ventricular dimensions, and ventricular function.

Electrocardiogram

Arrhythmia may become manifest during pregnancy with CHD. 24-hour ambulatory ECGs were performed in patients when they had abnormal electrocardiographic pattern; or in the setting of electrolyte that might affect the development of arrhythmia.

Pregnancy Data

Data relating to pregnancy were collected, including gestation at delivery and type of delivery, blood loss at delivery, birthweight, Apgar score and postpartum hemorrhage. Fetal echocardiographic have been used for the detection of congenital heart disease of fetuses, and cardiac ultrasound have been used for further confirmation in the newborns.

Statistics

Mean standard deviation was used for measurement analysis in this study. Student's t-test, chi-square or Fisher's precision probability method were used to evaluate the differences between the two groups, and $P<0.05$ was statistically significant.

Results

Patient characteristics

Thirty-one pregnant women with TOF were included in this study. All of them admitted to hospital were identified. The patients ranged in age from 19 to 39 years, 19 women were repaired TOF (aged between 22 and 35 years, median age was 28 years old), 12 women were untreated cases (aged between 19 and 39 years, median age was 26.5 years old). The treatment group of 19 patients all underwent surgical procedures included closure of the ventricular septum defect (VSD) by insertion of transannular patches, rendering the pulmonary valves incompetent, right ventricle infundibulectomy, and transannular enlargement of the right ventricular outflow tract. Except two patients with ventricular residual shunt on patch, the others completed repair after operation.

Cardiac and obstetric complications in two groups

Cardiac and obstetric characteristics in 31 pregnant women with TOF are shown in Table 1. Obstetric and cardiac complications were more frequent in the uncorrected group. The rate of prematurity was significantly higher in the uncorrected group (50% vs 5.26%, respectively). The frequency of spontaneous abortion was greater in the uncorrected group (16.67% vs nil, respectively). The percentage of small-for-gestational-age newborn was 41.67% in the uncorrected group and 10.53% in the corrected group. Compared with repaired group, the mean neonatal birth weight was significantly lower in the uncorrected group (P□0.001). However, the total days in hospital and blood loss at delivery were similar in both groups. The rate of postpartum hemorrhage was 10.53% in the corrected group and 8.33% in the uncorrected group, which was due to placenta praevia (2 vs 1 case, respectively) instead of abnormal blood coagulation. Congenital heart disease was noted in one baby with Patent ductus arteriosus (PDA) and patent foramen ovale (PFO) in the corrected group.

The cardiac complications were associated with maternal cardiac characteristics. Most of patients had good cardiac functional status with NYHA class of I-II in repaired TOF group, which significantly better than uncorrected group (63.16% vs 16.67%, respectively). Ten (83.33%) cases had cardiac function NYHA class III or more in uncorrected groups. Cardiac diameter and ventricular systolic function were assessed in all patients. This revealed right ventricle dilation in 12 (100%) uncorrected patients and in 9 (47.37%) corrected patients. One uncorrected patient with limited systolic function (EF = 31%, FS = 16%), and also with pulmonary arterial hypertension (PAH). In our study, the most common complications attributable to TOF were outflow tract and valve condition, ventricular level shunting with ventricular septal defect and arrhythmias. Pulmonic valvular stenosis was seen in all uncorrected patients and in 6 (31.58%) cases of corrected TOF. Of 19 corrected cases, there was residual shunt at VSD patches in 2 patients. According to the ECGs, we found that all uncorrected patients (100%) had right ventricular hypertrophy compared to 5 (26.32%) cases of repaired TOF. After the cardiac surgery, electrocardiogram returned to normal in 5 patients (26.32%), but complete right bundle branch block (CRBB) have been detected in 9 (47.37%) corrected patients. No other abnormal electrocardiogram was found between two groups.

Maternal and perinatal outcomes in the women with uncorrected TOF

In this study, 12 women were untreated cases; the detailed information is presented in Table 2. Among them, five (41.67%) woman were primigravid. Except for one patient with intrauterine fetal death undergone transvaginal complete curettage of uterine cavity, the mode of delivery in others were cesarean section. During the operation, CS was performed under general anesthesia in 6 patients, 4 cases under epidural anesthesia, and 1 patient under combined spinal-epidural anesthesia. Obstetric complications were investigated in all women, including miscarriages, premature labor, small for gestational age (SGA) and low birth weight infant at term (LBWI). Half of women (50%) with prematurity because of premature rupture of fetal membranes (PROM) and/or prenatal hemorrhage. The rate of SGA was 41.67% (n = 5). One case (NYHA class IV, severe pulmonary hypertension and limited systolic function), had to terminate pregnancy at 27+6 weeks due to heart failure. Then, she was transferred to the Department of Cardiology for further treatments and survived with careful care. Unfortunately, the baby died at the 7th day after birth due to neonatal pneumonia, septicemia and intracranial hemorrhage. The maternal mortality in this study was none. Neonatal mortality and fetal mortality were 3.23 % (1/31) and 6.45(2/31), respectively, which the mortality occurred in the uncorrected group.

Discussion

Tetralogy of Fallot (TOF) is a type of congenital heart disease (CHD) in which possesses the hemodynamic alterations characteristic of morphologic pulmonary arterial abnormality, ventricular dysfunction, right ventricular systolic dysfunction, right ventricular dilation, outflow tract obstruction, pulmonary hypertension[9]. After corrective surgery, the majority of young women with TOF survive into their reproductive age. But it is generally known that heart disease

constitutes a leading nonobstetric cause of maternal mortality especially in patients with those cyanotic and complex shunt lesions[4]. Previous studies on pregnant women with TOF showed that pregnancy carries a considerable risk to the women's status, and the adverse cardiovascular events may be associated with right ventricular dysfunction, severe pulmonary hypertension, and severe pulmonic regurgitation with RV dysfunction[10,11]. Right ventricular function parameters with abnormal uteroplacental Doppler flow (UDF) suggests that cardiac dysfunction contributes to defective placentation or placental perfusion mismatch and may explain the increased incidence of obstetric and neonatal complications[11].

In the past decades, CHD patients are increasingly reaching adulthood owing to remarkable diagnostic and therapeutic approaches. But TOF as serious complex and cyanotic congenital heart disease, women with uncorrected defects rarely survive into childbearing age and pregnancy. Some women with uncorrect TOF indeed successfully got pregnancy. However, because of the small number of these cases, the outcomes in these patients are not well studied, though it commonly thought that pregnancy adds extra load on the heart, and can damage cardiac function in a manner that leads both to increased maternal and perinatal morbidity[1–3,7]. In the current study, right ventricle dilation were found in all the patients without uncorrected TOF but present in less than half patients with corrected TOF. No incidence of thromboembolism and endocarditis were found in studied subjects, which may explain the overall good clinical outcomes in spite of different degrees of arrhythmias. Women with NYHA class > III have a relatively poor prognosis during pregnancy[12]. Of note, one uncorrected patient with NYHA class IV was the only patient with limited left ventricular systolic function and pulmonary arterial hypertension. This patient had to terminate pregnancy at 27+6 weeks due to ventricular failure. She survived with careful care, but the baby died at the post-partum period (the 7th day after birth). These results suggest that the degree of right ventricle dilation and NYHA classification are the most relevant factors for negative outcomes.

In the literature, it has been demonstrated that patients with corrected TOF still have a higher risk a poor pregnancy outcome because of the haemodynamic burden of pregnancy combined with residual cardiovascular lesions after repair[13,14]. Further problems after repair include residual or recurrent right ventricular outflow obstruction, right ventricular dilatation and residual VSD; and pulmonary regurgitation may lead to right ventricular dilatation and failure, atrial and ventricular arrhythmia, reduced exercise capacity[15]. In our study, there was residual shunt at VSD patches in 2 patients whose NYHA class all were grade III in the corrected group. And 6 patients (31.58%) had pulmonary regurgitation and about two-thirds of patients have different degrees of arrhythmia. Fortunately, none of our patients with corrected TOF showed pulmonary arterial hypertension and limited left ventricular systolic function. Following the surgical repair, electrocardiogram returned to normal in 5 patients (26.32%), and the right ventricle diameter and NYHA class were in normal range in more than half of them. Overall, women of childbearing age with repaired TOF may have lower pregnancy-related risks than those who did not undergoing pregnancy; the changes in ventricle dimensions and NYHA class are consistent with normal pregnancy adaptation[16].

Maternal condition and mortality has significant effects on fetal outcome in CHD patients[17]. Pregnant women with TOF were at high risk for maternal and neonatal complications as other types of heart disease, involving miscarriage, prematurity, premature rupture of membranes (PROM), preeclampsia, breech presentation, postpartum hemorrhage for the mothers; and small for gestational age, low birth weights, and cardiac anomalies for the newborns[4,18].Recently Ramage et al. reported 2114 births to women with ACHD (adult congenital heart disease) and suggested an association between several adverse neonatal and maternal outcomes and ACHD[19].They results showed that preterm births (<37 weeks gestation) were associated with 1.4 times higher odds among women with ACHD compared with those without ACHD.Women with ACHD also had higher odds of having a preterm birth at less than 32 weeks'gestation. Almost 12.8% of women with ACHD delivered an SGA infant compared with 8.7% of women without ACHD. Similar to the results of this study, all the patients in our study have survived although most all of them suffered varying degrees of cardiac and obstetric complications, and the complications were more frequent in the uncorrected group. In addition, the rate of prematurity, miscarriage and SGA was significantly higher in the uncorrected group. There is a 50% incidence of prematurity in the uncorrected patients. Due to low maternal cardiac output, intrauterine growth restriction may unavoidably occur[20]. The mean birth weight centile was significantly lower, and the small for gestational age was a common occurrence (41.67%) in pregnancy women with unrepaired TOF. In consideration of high complication risks, woman with cardiac disease may be safer with a cesarean section delivery to avoid prolonged labor or any pushing[21].In this study, one patient with intrauterine fetal death undergone transvaginal complete curettage of uterine cavity, other uncorrected patients delivered by cesarean section under combined spinal epidural anesthesia, epidural anesthesia or general anesthesia. We assumed that the successful outcomes resulted from the absence of thromboembolism, severe hypertension, and cardiac failure. Although one case suffered with hypertension and cardiac failure, she was survived with professional care. Women at highest risk can benefit from preconception counseling and close clinical monitoring during pregnancy[19]. Careful interdisciplinary management among the cardiologist, obstetrician, anesthetist, and neonatologist, and detailed plans for delivery may have improved the prognosis[22].

Conclusions

In summary, regnancies with TOF present with a high-risk of cardiac and obstetric complications, especially in those who did not received repair surgery. Maternal and neonatal risks appeared to be associated with the degree of ventricular dilatation heart, functional classifications, serious cardiac arrhythmias and pulmonary hypertension. Absence of thromboembolism and heart failure are the favorable factors in the pregnant woman with TOF.

Declarations

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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Tables

Table 1. Comparisons of clinical characteristics, cardiac and obstetric complications, and outcome of pregnancy in TOF patients with or without surgical repair

Parameters	n (%)	Corrected (n=19)	Uncorrected (n=12)	p-Value
NYHA-FC				
I-II	14 (45.16)	12 (63.16)	2 (16.67)	0.031
III–IV	17 (54.84)	7 (36.82)	10 (83.33)	
Left ventricular systolic function				
Normal	30 (96.77)	19 (100)	11 (91.67)	0.397
Dysfunction	1 (3.23)	0	1 (8.33)	
Right ventricle dilation				
Normal or mild	10 (32.26)	10 (52.63)	0	0.004
Moderate or severe	21 (67.74)	9 (47.37)	12 (100)	
Valve condition				
Pulmonic valvular stenosis	16 (51.61)	4 (21.05)	12 (100)	<0.001
Pulmonic regurgitation	6 (19.35)	6 (31.58)	0	0.059
Tricuspid regurgitation	13 (41.94)	10 (52.63)	3 (25)	0.158
Mitral regurgitation	1 (3.23)	1 (5.26)	0	-
Arrhythmias				
normal	5 (16.13)	5 (26.32)	0	0.128
Right ventricular hypertrophy	17 (54.84)	5 (26.32)	12 (100)	<0.001
CRBB	9 (29.03)	9 (47.37)	0	0.005
IRBBB	6 (19.35)	3 (15.79)	3 (25)	0.653
Sinus tachycardia	3 (9.68)	2 (10.53)	1 (8.33)	-
I°AVB	2 (6.45)	1 (5.26)	1 (8.33)	-
APB	1 (3.23)	1 (5.26)	0	-
VPB	2 (6.45)	2 (10.53)	0	-
Pulmonary hypertension	1 (3.23)	0	1 (8.33)	-
Aortopulmonary collateral vessels	3 (9.68)	0	3 (25)	-
Pericardial effusion	2 (6.45)	0	2 (16.67)	-
Outcome of Pregnancies				-
Miscarriages	2 (6.45)	0	2 (16.67)	-
Prematurity	7 (22.58)	1 (5.26)	6 (50)	0.007
SGA	7 (22.58)	2 (10.53)	5 (41.67)	0.078
LBWI	1 (3.23)	0	1 (8.33)	-
CHD of newborn	1 (3.23)	1 (5.26)	0	-
Fetal death	2 (6.45)	0	2 (16.67)	-
Neonatal death	1（3.23）	0	1（8.33）	-
Maternal death	0	0	0	-
Postpartum hemorrhage▲	3(9.68)	2(10.53)	1(8.33)	-
Blood loss at delivery (ml) #	31	394.4±241.2	456.3±365.7	0.586
Mean neonatal weight (kg) #	28	2941.842±352.720 （n=19）	1831.722±873.232 (n=9)	<0.001
HOD (day) #	31	7.947±3.503	7.750±2.454	0.866

*Continuous data are presented as mean and range; nominal data, as number of patients and percentage of sample; Postpartum hemorrhage▲: blood loss >500ml atvagin delivery or >1000 ml at Caesarean section. NYHA-FC: cardiac function grading (New York Heart Association); CRBB: complete right bundle branch block;IRBBB: incomplete right bundle branch block;AVB: atrioventricular block; VPB: ventricular premature beat; APB: atrial premature beat; SGA: Small for gestational age; LBWI: Lov Birth Weight Infant at Term; CHD: Congenital heart defect; HOD: hospital day (total days in hospital); #: data are expressed as Mean ±SD

Table 2. Maternal Hemodynamic Features and Obstetric Outcomes in Pregnant Woman with Uncorrected Tetralogy of Fallot

#	Age	G/P	NYHA-FC	RVdiameter (mm)	RVAW (mm)	RV outflow tract	PA (mm)	VSD (mm)	Other	LVSD (%)	Arrhythmia▲	Obstetric complication	Mode of delivery	Anaesthesia
1	26	G5P1	III	30	5	4	12	20	*Collat. circ.	EF=72 FS=40	-	SGA	Caesarean section: 38+3weeks	General anaesthesia
2	26	G1P0	II	31	9	17	15	16	ASD TR PDA	EF=80 FS=36	-	Prematurity	Caesarean section: 35+6 weeks	General anaesthesia
3	35	G5P2	III	35	10	11	14	-	-	EF=50 FS=28	I°AVB	SGA,Prematurity	Caesarean section: 35 weeks	Epidural analges
4	19	G1P0	III	33	10	9	17	20	-	EF=60 FS=30	-	Prematurity	Caesarean section:33 weeks	General anaesthesia
5	39	G8P1	III	30	13	15	24	20	-	EF=58 FS=31		Prematurity	Caesarean section:36+1 weeks	General anaesthesia
6	23	G2P1	II	28	10	11	22	22	-	EF=56 FS=29		SGA□LBWI	Caesarean section:38 weeks	Epiduralanaesthe
7	31	G3P2	IV	30	14	13	17	17	PH *Collat. circ.	EF=31 FS=16	-	Prematurity	Caesarean section:27+6weeks	General anaesthesia
8	27	G2P0	III	36	12	8	11	15	Right aortic arch	EF=58 FS=29	IRBBB	Prematurity	Caesarean section: 34+2 weeks	Epiduralanaesthe
9	20	G1P0	III	38	11	9	15	17	*Collat. circ.	EF=58 FS=30	Sinus tachycardia	SGA	Caesarean section:36+6weeks	Combined spinal epidural
10	36	G1P0	III	37	9	10	18	22	TR	EF=70 FS=38	IRBBB	Miscarriages	Vaginal delivery: 9 weeks	unknown
11	30	G2P0	III	24	10	8	8	22	ASD	EF=67 FS=36	-	Miscarriages	Caesarean section:16+6weeks	Epiduralanaesthe
12	23	G1P0	III	27	10	8	13	14	Right aortic arch	EF=67 FS=36	IRBBB	SGA	Caesarean section:37weeks	General anaesthesia

G/P: Gravidity and parity history; NYHA-FC: cardiac function grading (New York Heart Association);RV: Rightventricular; PA: pulmonary artery; RVAW:right ventricular anterior wall; VSD:ventricular septal defect;ASD:atrial septal defect; PDA: Patent ductus arteriosus; TR: tricuspid regurgitation; PH:Pulmonary hypertension;LVSD: left ventricular systolic function; AVB: atrioventricular block;IRBBB: incomplete right bundle branch block;SGA: Small for gestational age;LBWI: Low Birth Weight Infant at Term

*Collat.circ.: Aortopulmonary collateral vessels; Arrhythmia▲:All patients showed right ventricular hypertrophy.