Maternal and Perinatal Outcomes in Uncorrected Tetralogy of Fallot

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Abstract

Background: Tetralogy of Fallot (TOF) is the most common congenital heart disease in the population. Correction of TOF during infancy or childhood may increase the quality of patient's life. Uncorrected TOF may cause further complications later on. Pregnancy with uncorrected TOF may cause complications on both maternal and fetal sides.

Objective: to analyze maternal and perinatal outcomes in patients with uncorrected TOF during pregnancy.

Methods: This is a retrospective study. A total of 8 pregnant women diagnosed with TOF registered in the Obstetric-Cardiac unit in 3 years (2016-2018). Medical records were reviewed for clinical assessment, echocardiography results, and therapy during hospitalization. Patients were contacted by telephone to provide an obstetric history, including details of pregnancy and delivery. Five of 7 patients able to be contacted, and home visits were done to evaluate their conditions.

Results: There were 8 pregnant women with uncorrected TOF. Most cases (87,5%) were first diagnosed during pregnancy and delivery. Intra-Uterine Growth Restriction (IUGR) and abortion (62.5% and 25%, respectively) were the most obstetric complications. Cardiac complications were cardiogenic shock (12.5%), thromboembolic (12.5%), and various degree of heart failure (62.5%). The number of Small for Gestational Age (SGA) was 66.7%. Incidence of congenital heart disease (CHD) in the fetus was 20%. One death case and 2 abortions from a total of 8 cases were found.

Conclusion: TOF may cause many maternal and fetal complications. The most common maternal complications are heart failure, cardiogenic shock and thromboembolic, while perinatal complications include IUGR, SGA and abortion.

Keywords*: Uncorrected Tetralogy of Fallot, pregnancy, outcome, complication*

Introduction

Tetralogy of Fallot (TOF) is the most common form of congenital heart disease (CHD), representing 7-10% of all CHDs. It is characterized by a ventricular septal defect (VSD), overriding aorta, pulmonary stenosis, and right ventricular hypertrophy[(1)]. The incidence of CHD in Indonesia was relatively high, with 9 neonates per 1.000 live births and an estimated 40.500 babies born with CHD in Indonesia per year [(2)]. The discrepancy between the augmentation of cases per year and the number of surgeries contributed to the increase of uncorrected TOF.

If uncorrected TOF women reach adulthood and plan to conceive, a multidisciplinary team's supervision is needed during pregnancy and delivery. This study

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aims to analyze the maternal and perinatal outcomes in patients with uncorrected TOF during pregnancy. It consists of cases with uncorrected TOF in pregnancy that experienced delays in the diagnosis, and some were mismanaged. We hope this study could strengthen team works between obstetrician, cardiologist, a congenital cardiac surgeon, and anaesthetist in managing congenital heart disease in pregnancy.

Materials and Methods

This is a retrospective study. A total of 8 pregnant women diagnosed with TOF registered in the Obstetric-Cardiac unit in 3 years (2016-2018). Medical records were reviewed for clinical assessment, echocardiography results, and therapy during hospitalization. Patients were contacted by telephone to provide an obstetric history, including details of pregnancy and delivery. Five of 7 patients able to be contacted, and home visits were done to evaluate their conditions. Ethical approval obtained from Universitas Airlangga Academic Hospital, Surabaya Indonesia

Results

A total of 8 patients with TOF were identified. The characteristic of these patients were summarized in table 1. The mean age of the patients were 22.1 years old, all of them had never undergone surgery before. Diagnosis of TOF was late to be diagnosed, 87.5% cases were found during pregnancy and post-partum. Elective caesarean section (CS) was performed in 5 patients (71.4%), whereas forceps extraction and curettage were performed in 1 patient (14.3%).

Table 1. Maternal Characteristic of Pregnancy with Uncorrected TOF

Characteristic	Frequency (%)
Maternal Age 20 – 30 years old Mean age : 22,1 years old	8 (100)
Parity Primigravida	8 (100)
Time of Diagnosis Pre conception Gestational age < 20 w Gestational age > 20 w Post-partum	 1 (12,5) 3 (37,5) 3 (37,5) 1 (12,5)
Mode of Delivery (n=7) Cesarean Section Forceps Curettage	 5 (71,4) 1 (14,3) 1 (14,3)
Methods of contraception (n=7) IUD Sterilization	 1 (14,3) 6 (85,7)
Laboratory (n=8) Mean Hb : 15,35 g/dL Mean Hematocrit: 47,45%	
Oxygen Saturation (n=8) < 85% 85-90% >90%	 1 (12,5) 2 (25) 5 (62,5)

Obstetric and cardiac complications during pregnancy until post-partum periods were summarized in table 2. Since all women had never undergone cardiac surgery, heart failure was the most common complication, with varying degrees of DCFC. Most of them presented in DCFC II (62.5%). Cardiogenic shock was found in 1 patient (12.5%), occurring immediately post-delivery. Thromboembolic was also found in 1 patient (12.5%). On the other hand, intra uterine growth restriction (IUGR) was recorded in 62.5% cases, and became the highest obstetric complication in this group of study. Abortion was the second most common complication after IUGR. One case of abortion occurred spontaneously, and the remaining was elective termination during the first trimester.

Table 2. Cardiac and Obstetric Complications in maternal side

Complications	Frequency (n,%)
Cardiac	
Heart failure NYHA II	5 (62,5)
Heart failure NYHA III	2 (50)
Heart failure NYHA IV	1 (12,5)
Thromboembolic	1 (12,5)
Cardiogenic shock	1 (12,5)
Obstetric	
PROM	1 (12,5)
Preeclampsia	1 (12,5)
Abortion	2 (25)
IUGR	5 (62,5)
Oligohydramnion	1 (12,5)

Seven of 8 patients presented to the hospital during pregnancy, in a varying gestational age. Profile of pregnant women was summarized in table 3. There were 2 patients whom was diagnosed with TOF in the first trimester (A-1 & F-6), and before pregnancy (G-7). Even the pregnancy could endanger them, they were determined to continue the pregnancy. We did multidiscipline conference and did closely monitor the patients, and the pregnancy terminated in appropriate time.

Table 3. Maternal and perinatal outcome

Initial	Time of diagnosis	Hb (g/dl) SO2 (%)	HF NYHA	Indication of Termination	Time of termination (weeks)	Birth weight (g) BS (weeks) LS	MOD	Perinatal Complication	Last Condition
A-1	Pregnant (5/6w)	19,3 78	IV	Spontaneous Abortion					Death
B-2	Pregnant (26-27 w)	15,6 93	II	IUGR	29/30 w	1000 32; p<10	CS	ASD, RDS, Gastric outlet obstruction	NYHA II, SO2 71%

Cont... **Table 3. Maternal and perinatal outcome**

C-3	Pregnant (10/11 w)	14,3 93	II	PROM + IUGR	36 w	2100 36; p10-25	CS	(-)	NYHA II, SO2 94%
D-4	Pregnant (36/37 w)	11,9 98	II	IUGR + Oligohidramnion	36/37 w	2650 38; p10-25	CS	(-)	NYHA II, SO2 98%
E-5	Pregnant (33/34 w)	16,4 86	III	IUGR	33/34 w	1100 33; p<10	CS	RDS, EOS	NYHA II, SO2 80%
F-6	Pregnant (6/7 w)	17,4 86	III	DCFC III	7/8 w		Curettage		Loss of Follow Up
G-7	Before pregnant	16,2 92	II	Preeclampsia + IUGR	31/32 w	1000 32; p<10	CS	NEC, RDS	NYHA II, SO2 95%
H-8	Post partum	11,7 98	II	Suspect CHD & In-labor	38 w	2000 38; p<10	Forceps	(-)	Loss of Follow Up

BS: Ballard Score; LS: Lubchenco score; MOD: Mode of Delivery; CS: Cesarean Section; ASD: Atrium septal defect; RDS: Respiratory Distress Syndrome; EOS: Early Onset Sepsis; NEC: Necrotizing Entero Colitis; NYHA: New York Heart Association

One pink Fallot patient (D-4) adapted well during pregnancy. There was no dyspnea, orthopnea, or limitation of activity recorded. Diagnosis of TOF was accidentally found due to her confession in the late pregnancy, and then she was referred to the tertiary hospital for further management. The other two patients complicated with heart failure since the first trimester (F-6 & A-1) and ended up with pregnancy termination and spontaneous abortion. Two cases (B-2 & E-5) were referred to tertiary hospitals due to fetal compromise.

A total of 6 deliveries occurred within 30 months. All babies were life births, and 5 of 6 babies (83.3%) were delivered prematurely. One neonatal death (16.7%) occurred during the 7th day of hospitalization. Multiple congenital anomalies were noted in this baby, including atrial septal defect (ASD) and gastric outlet obstruction.

The correlation between maternal presentation and perinatal outcomes was summarized in table 4. Low levels of oxygen, high concentrations of haemoglobin (Hb), and degree of heart failure (NYHA) impacted pregnancy outcomes. We noted 2 abortions happened in the worst condition among the group. During hospitalization, some neonatal complications due to prematurity occurred, such as respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), and early onset of sepsis (EOS). The incidence of RDS was 40%, whereas NEC and EOS occurred in 20% of infants.

Table 4. Perinatal Outcomes Characteristic

	LB, n(%)	**Premature, n(%)**	**SGA, n(%)**	**NND, n(%)**	**Mean birth weight, kg**
Frequency (n=6)	6 (100)	5 (83,3)	4 (66,7)	1 (16,7)	1,641

LB: life birth, SB: still birth, SGA: small for gestational age, NND: neonatal death

Among 8 patients, there was 1 maternal death; hence the case fatality rate was 12.5%. The mean length of stay (LOS) was 8.25 days. All women needed intensive care, but none of them needed a ventilator. Pregnancy did interfere cardiac condition of uncorrected TOF women. 87.5% of patients were discharged well, but there was a significant decrease in oxygen saturation in 2 patients after 4 months and 2 years of follow up.

Discussion

TOF has various cyanosis degrees that require urgent surgical intervention in early life to cyanotic form that often undiagnosed or late to be diagnosed [4]. All patients in this study were diagnosed in adulthood or during the pregnancy and delivery process, whereas in other studies, 30-100% of cases of TOF had been diagnosed and repaired before pregnancy[3], [5], [6]. Hemodynamic changes in pregnancy and delivery may cause clinical deterioration due to an increase in right to left shunt and worsening of cyanosis. Moreover, the autotransfusion process, sympathetic activation due to pain, or obstetrical haemorrhage will put more strain on an already compromised heart, leading to increase right-to-left shunt, and worsening of cyanosis.

During pregnancy, the most common cardiac complication was arrhythmias (4,7%) and heart failure (1,6%) in pregnancy with congenital heart disease. Nonetheless, cyanotic heart disease (corrected or uncorrected) had a higher risk of cardiac complications, with OR 3,0 [7]. Many studies indicate that better maternal outcomes can be achieved in patients with uncorrected or palliated TOF or incomplete repair and residual cyanosis. The heart failure rate was higher in an uncorrected group compared to the repaired group (40% vs 2% respectively). Moreover, the uncorrected group's maternal mortality rate was 4-12 times higher (4-12% vs 0%) compared to corrected TOF [7]. On the other hand, all women in our study were at least in DCFC II; hence the heart failure rate was 100%. Other cardiac complications reported were thromboembolic in 12,5% and cardiogenic shock in 12,5%.

Cardiac complications in our study were relatively high. This could be caused by inadequate preconception counselling. A Scoring system to calculate the risk of cardiac complications during pregnancy in CHD women have been developed. If we calculated the risk of these women in pregnancy, we would find at least 7,5% risk of cardiac complication (ZAHARA score) could rise in such patients during pregnancy[7]. Assessment of the risk ideally conducted preconception period, and medication needs can be determined before pregnancy to minimize complications. Preconception counselling included clinical assessment, echocardiography, blood gas analysis, and electrocardiography in determining whether the pregnancy is contraindicated or not and to determine the need for surgery before pregnancy. The decisions should be made by a multidisciplinary team in a tertiary hospital[8].

Our country's problem was a late diagnosis of TOF seemed to cause less optimal management and monitoring of the experts. We missed preconception counselling and regular cardiologist visits as WHO recommends every 1 or 2 months to visit a cardiologist in WHO maternal class III group (uncorrected TOF)[8]. Also, fetal echocardiography should be conducted in the second trimester to screen congenital heart anomaly in the fetus. We had one case where the diagnosis of fetal ASD had not been made during pregnancy. Monitoring of fetal during the third trimester was aimed to screen whether the growth was restricted or not.

There was no consensus on the exact time of delivery for CHD women. Clinical presentation of the patient and fetal well-being were determinant factors to do the termination. Five pregnant women in our study were decided to terminate by CS due to obstetric indication (IUGR). The preferred mode of delivery is vaginal delivery that should take place in a tertiary centre with specialist multidisciplinary team care. Vaginal delivery is associated with lower blood loss and infection rate compared to caesarean delivery. On the other hand, caesarean delivery increases risk of venous thrombosis and thromboembolic, so that in general, CS is performed due to obstetrical indication [8]. It is recommended to use lumbar epidural analgesia during the delivery process. It reduces pain-related elevations of sympathetic activity, reduces the urge to push, and reduces cardiac output 37% during delivery [8], [9].

Previous research concludes that maternal hematocrit is more significant than 60%, oxygen saturation is less than 80%, and haemoglobin level > 18 g/dL were poor prognostic factors. These pregnant women were

associated with adverse fetal outcome [3], [9]. Another study explained that the chance of a pregnancy resulting in a live birth decreases to 12% if oxygen saturation was less than 85% or 8% if haemoglobin level > 20 g/dL [6]. Our study was consistent with the previous study. We had one case of spontaneous abortion whose maternal oxygen saturation was 78%, and haemoglobin level was 19,3 g/dL. The rate of abortions in our study (25%) was similar to the study in India (28,5%) [5]. All abortion cases occurred in uncorrected TOF women.

Some predictors of adverse neonatal outcomes were NYHA class greater than II, cyanosis, maternal left-ventricular obstruction, maternal smoking, maternal age under 20 years or over 35 years, multiple gestations and anticoagulation during pregnancy [10]. Siu *et al.* identified that the rate of neonatal complications has significantly increased in women with heart disease. Neonatal complications occurred in 18% of pregnancies. Preterm delivery occurred in 15%; fetal growth restriction occurred in 4%, respiratory distress syndrome (RDS) or intraventricular haemorrhage in 2% and neonatal death in 3% of pregnancies [11].

The rate of prematurity and small for gestational age (SGA) babies in our study were higher (66,7%), compared to the previous study in India and America, 30% and 40% respectively [3], [5]. The mean birth weight in our study was 1,64 kg. This number was similar to a study in India in an uncorrected TOF group of 1,62 kg. Preterm delivery was higher in our study (83,3%) than in other studies in India (40%). Termination in premature babies was common in our study due to fetal growth restriction antenatal, whereas the causes of prematurity in India had not been explained. A higher number of prematurity may result in a greater incidence of neonatal complication in 5 babies, such as RDS in 60%, necrotizing enterocolitis (NEC) in 20%, and early onset of sepsis (EOS) in 20%.

The risk of congenital heart disease (CHD) in the offspring of women with heart disease is increasing compared to the general population (1%). A previous study suggested various risks in lesion-specific and parents inherited. If the mother had TOF, the risk of CHD increased to 2,6%. Among 5 babies delivered in our hospital, we reported 1 case of ASD in the baby; hence, CHD incidence in our study was 20%. Moreover, previous medication before pregnancy could adversely affect the fetus (e.g., ACE inhibitors, warfarin, and statins). There was no medication before pregnancy in the woman whose baby had congenital heart disease. During hospitalization, she diagnosed with gastric outlet obstruction, and she died on the 7th day of care. Thus, neonatal death was 16,7%.

There is limited data on the effects of pregnancy on long-term outcomes in women with heart disease. One recent study showed a significant increase in sub pulmonary ventricular size persisting after pregnancy in patients with TOF [12]. Unfortunately, TOF patients involved were corrected TOF. There was no further study in the uncorrected group since the TOF patients' surgical intervention had been improved. All the women in our study survived during hospitalization and were discharged in a stable condition. Follow up and a home visit was done for 5 patients, but 2 of them were lost for follow up. The clinical condition of these 5 patients was DCFC II in 4 patients, DCFC I in 1 patient (pink Fallot). We did evaluate the oxygen saturation in every patient, and we found 2 patients had a significant decrease (from 86% to 80% within 4 months, and from 93% to 71% within 2 years). Nonetheless, they all refused to do the further evaluation in our hospital.

Conclusion

Uncorrected TOF leads to many complications that may arise in pregnancy and the outcomes. The most frequent maternal complications are heart failure, cardiogenic shock and thromboembolic, while perinatal complications involve IUGR, SGA and abortion.

What is already known

Proper multidisciplinary management is required for a better pregnancy outcome of the mother and the fetus.

What this paper adds

Knowing that many uncorrected TOF cases were to be found in developing countries, in which may cause many complications to the mother and the fetus, proper diagnosis in early pregnancy during antenatal care and multidisciplinary management are recommended.

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References

1. Bailliard F., Anderson R H. (2009). Tetralogy of Fallot. *Orp J Rare Disease*: 4(2): 1-10
2. Rahajoe A U. Management of patients with congenitally malformed hearts in Indonesia. Cardiol Young 2007; 17: 584-588
3. Veldtman G R., Connolly H M., Grogan M., Ammash N M., Warnes C A. Outcomes of pregnancy in women with tetralogy of Fallot. J Am Coll Cardiol 2004; 44(1): 174-180
4. Liberman R F., Getz K D., Lin A E., Higgins C A., Sekhavat S., Markenson G R., *et al*. Delayed diagnosis of critical congenital heart defects: Trends and associated factors. Am Academy Pediatrics 2014; 134(2): 373-381
5. Kaur H., Suri V., Anggarwal N., Chopra S., Vijayvergiya R., Talwar K. Pregnancy in patients with tetralogy of Fallot: Outcome and management. World J Pediatric Congenital Heart Surg 2009; 1(2): 170-174
6. Gelson E., Johnson M. Effect of maternal heart disease on pregnancy outcomes. Expert Rev Obstet Gynecol 2010; 5(5): 605-617
7. Drenthen W., Boersma E., Balci A., Moons P., Roos-Hesselink JW., *et al*. Predictors of pregnancy complications in women with congenital heart disease. Euro Heart J 2010; 31: 2124-2132
8. Regitz-Zagrosek V, Lundqvist CB, Borghi C, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J.2011; 32(24):3147-97
9. Koos BJ. Management of uncorrected, palliated and repaired cyanotic congenital heart disease in pregnancy. Prog Paediatr Cardiol 2004;19:25-45
10. Siu SC., Sermer M., Colamn J. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001; 104: 515-521
11. Siu SC., Colman JM., Sorensen S., *et al*. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. Circulation 2002; 105: 2179-2184
12. Uebing A., Arvanitis P., Diller G P., Babu-Narayan S V., Okonko D., Koltsida E., *et al*. Effect of pregnancy on clinical status and ventricular function in women with heart disease. Int J Cardiol 2010; 139: 50-59