ORIGINAL ARTICLE

SHORT AND MIDTERM OUTCOME OF FALLOT'S TETRALOGY REPAIR IN INFANCY: A SINGLE CENTER EXPERIENCE IN A DEVELOPING COUNTRY

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Background: Primary repair of ToF between 3–12 months is the preferred mode of treatment worldwide, with low surgical mortality. This study reviews our experience of ToF repair in infancy and its short and midterm outcomes in a single centre from a developing country. **Methods:** Data of all patients with Tetralogy of Fallot repair during infancy from January 2007 to Feb 2018 was reviewed. Preoperative, operative, and postoperative data was analysed. Outcome of the infants was assessed through discharge/death, low cardiac output syndrome (LCOS), prolonged intubation, duration of cardiac intensive care unit (CICU) and hospital stay. **Results:** Forty-four patients who underwent TOF repair in infancy during this period were included. The mean age and weight were 9.39±2.32 and 7.20±1.30 respectively, 77.3% (34 patients) were male, 68.18% (30 patients) had saturation >75%. Mean intubation period was 4.05±6.58 days, 12 (27.3%) patients developed LCOS, mean cardiopulmonary bypass (CPB) time, aortic cross clamp (ACC) time and ionotropic score were 133.52±62.4, 98.66±58.62 and 33.27±71.13 respectively. Mean CICU and hospital stay was 6.60±7.18 and 12.05±7.74 respectively. Five (11.3%) patients expired in postoperative period. Baseline saturation ≤75% is independent risk factor for LCOS and prolong intubation period. In the last six years our mortality decreased to 8% from 15.7% during the previous six years, while our mean intubation duration, CPB time, ACC, hospital stay and CICU stay have all shown improvement. **Conclusion:** TOF repair during infancy is safe procedure in expert hands with acceptable morbidity and mortality. Baseline saturation ≤75% is independent risk factor for LCOS and prolonged intubation period. Last six years have shown considerable improvement in our surgical morbidity and mortality due to improvement in surgical expertise.

Keywords: Tetralogy of Fallot repair; Low cardiac output syndrome; Congenital heart disease surgery; Operative mortality ToF

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INTRODUCTION

Surgical repair of Tetralogy of Fallot (ToF) has undergone revolutionary changes over the course of time.[1] Earlier indications for TOF repair like, hyper cyanotic spells and oxygen saturation of <75% are no longer in practice. Primary repair between 3–12 months is the preferred mode of treatment in developed countries.[2] However, in developing countries this is not common practice due to multiple factors including late diagnosis, financial constraints, and relatively higher morbidity and mortality due to lack of medical and surgical expertise. Due to these reasons data from developing countries is still lacking regarding morbidity and mortality of TOF repair in infancy. This study reviews our experience of TOF repair in infancy and its short and midterm outcomes in a single centre from a developing country.

MATERIAL AND METHODS

After approval from institutional ethical review committee, all patients with a diagnosis of TOF with pulmonary stenosis, who underwent primary repair between January 2007 and February 2018 at Aga Khan University Hospital, Karachi were identified from hospital data base. We excluded patients with associated anatomic defects such as absent pulmonary valve syndrome, atrioventricular septal defect, or pulmonary atresia.

Data was collected on a preformed questionnaire. It included basic demographic parameters (age at the time of surgery, sex, weight and baseline saturation). We defined severe TOF as patient with TOF having saturation ≤75%.

Echocardiographic data included pulmonary valve annulus z-score, right ventricular outflow tract obstruction (RVOTO), pulmonary regurgitation[3], concomitant cardiac defects, Operative parameters analysed were operative technique, cardiopulmonary bypass time (CBP), aortic cross clamp time (ACC), and hemodynamically significant residual lesions and residual RVOTO[4] on intraoperative trans-epicardial echocardiogram. Postoperative CICU data included length of ICU stay, duration of mechanical ventilation, inotropic score (high ionotropic score ≥20)[5,6], postoperative conduction abnormalities such as junctional ectopic tachycardia (JET)[7] or complete heart block, low cardiac output syndrome (LCOS)[8] and death in postoperative period. Based on published data, we defined prolonged CICU stay as ≥7 days, and prolonged mechanical ventilation as ≥48h.[9] Echocardiographic data, morbidity and mortality was again assessed at short term follow–up (within one month of surgical repair) and midterm follow-up (at one year after surgical repair).

Data was analysed using SPSS version 19. Standard descriptive statistical methods were used. Data are described as frequencies or medians with ranges, as appropriate. To assess differences between groups, Student's t test for continuous data and the chi-square for categorical data were used. Univariate analysis was done to determine risk factors for mortality. To analyse difference between two eras of surgical experience, namely first and next six years, Mann -Whitney U test was used. A p value <0.05 was considered statistically significant.

RESULTS

Based on our inclusion criteria a total of 44 patients were identified. Table-1 shows the demographic, clinical feature and base line echocardiographic findings of the study population. In 41 patients (93.2%) transannular patch technique used, while 3 patients (6.8%) had valve sparing surgery. Intraoperative trans-epicardial echocardiogram showed residual hemodynamically insignificant lesions in 24 (59%) patients, while four patients (9.1%) with significant residual lesion required a repeat bypass run. Mean CPB time and ACC time were 133.52±62.4 and 98.66±58.62 respectively. Twenty-three (52.3%) patients had mild residual RVOTO on trans-epicardial echo intra-operatively. In the postoperative period (Table-2), 7 patients (15.9%) developed JET, 4 (9.1%) of them treated with amiodarone, 2 (4.5%) with pacing and one with cooling only (2.3%).

Three patients went into complete heart block, of whom 2 (4.5%) required permanent pacemaker implantation. Twelve (27.3%) patients developed LCOS in the post-operative period. Two patients (4.5%) stayed in the hospital for more than 30 days: one stayed for 34 days because of sepsis, and the other stayed for 43 days, the later was admitted with hyper-cyanotic spell, had respiratory complications during stay and postoperatively developed low cardiac output syndrome leading to his death. Mean postoperative ionotropic score and duration of intubation were 33.27±71.13 and 4.05±6.58 days respectively. Mean CICU and hospital stay were 6.60±7.18 and 12.05±7.74 respectively. Five patients (11.4%) died in the early postoperative period. At short term follow-up data of remaining 39 patients, one patient continued to have intermittent junctional rhythm although he was hemodynamically stable. Echocardiography showed majority 17 (43.5%) to have mild pulmonary regurgitation, mild to moderate residual RVOTO was present in 27 (69.2%) patient, mild to moderate RV dysfunction and created patent foramen ovale (PFO) was present in 27 (69.23%) and 24 (64.1%) patients respectively. Five patients were lost to follow up, making data of only 34 patients available at midterm analysis. Number of patients with mild regurgitation decreased to 9 (26.4%), while moderate and severe PR was present in 10 (29.4%) and 8 (23.5%) patients respectively. 23 (67.6%) patients had mild to moderate RVOTO. We divided our study period in two eras of six years each of initial and subsequent experience, to compare surgical morbidity and mortality (Table 3). Nineteen (43.18%) patients had ToF repair in the initial 6 years, while 25 (56.8%) patients had this surgery during infancy in the last six years. Although our surgical mortality improved from 15.7% (3 patients) patients to 2 (8%) patients in last six years, but there was no statistical significance (p<0.30). In the last six years our mean intubation duration decreased to 2.84±3.85 from 5.42±8.95 (p<0.056), CPB time decreased from 155.79±69.61 to 118.20±50.97 (p<0.003), aortic cross clamp time decreased from 117.42±75.55 to 86.40±36.06 (p<0.019), hospital stay decreased to 10.48±6.38 from 14.05±8.90 (p<0.046) and CICU stay decreased from 8.74±9.49 to 4.84±4.11 (p<0.015). The ionotropic score during last six years has increased from 29.16±28.59 to 36.80±91.70 (p<0.046), due to one patient who had a very high ionotropic score of 465.

The data was also compared for oxygen saturations at base line with outcome, ionotropic score, low cardiac output syndrome (LCOS), hospital stay, CICU stay and intubation period. We divided patients into two groups; those with saturation ≤75% were regarded as severe TOF and ≥75% as less severe TOF. In patients with saturations ≤75% group there were 14 (31.8%) patients, out of which 3 expired (21.4%), while in those with saturation >75% 2 patients expired (6.6%). Comparing saturation with ionotropic score it was found that in patients with saturations ≤75% group 7 (50 %) patients had high ionotropic of >20 as compare to those

with saturation >75% in which on only 9 (30%) patient with high ionotropic score. However, both these comparisons were not found statistically significant (p=0.304 and 0.199). Eight (57.1%) patients developed LCOS in patients with saturations ≤75% group as compare to 4 (13.3%) in those with saturation >75 (p<0.002). On comparing hospital stay and CICU stay with saturation, 8 (57.1) patients with saturations ≤75% group and 14 (46.7%) patient in those with saturation >75% found to have prolong hospital stay of ≥10 days having p<0.517. Similarly, patient with the saturations ≤75% group 6 (42.9%) had prolong CICU stay of ≥7days as compare to 6 (20%) patient in those with saturation >75%, (p<0.113).

On comparing saturation with intubation period, it was found that 9 (64.3%) patient with saturation ≤75% group had prolonged intubation period of >48 hours as compare to 9 (30%) patients those with saturation >75%, p<0.031. On univariate analysis of factors such as age, gender, weight height, PV z score, ACC time, CPB time, prolonged intubation of ≥48 hours, long CICU stay with outcome showed no statistical significance.

Table-1: Demographic, clinical and preoperative Echocardiographic parameters

Characteristics	
Age (months) mean±SD	9.39±2.32
Gender (n, %)	
Male	34 (77.3%)
Female	10 (22.7 %)
Weight (Kg) mean +SD	7.20±1.30
Height(cm) mean ±SD	69.10±5.69
Saturation (n, %)	
<75%	14 (32%)
>75%	30 (68%)
Hypercyanotic spell (n, %)	8 (18.2%)
Yes	36 (81.8%)
No	
PV at baseline (n, %)	
Normal (z score ≥-2)	11 (25%)
Mild hypoplasia (z score -2 to -3)	11 (25%)
Moderate hypoplasia (z score -3 to -4)	18 (40.9%)
Severe hypoplasia (z score ≤-4)	4 (9.1%)
PV stenosis gradient severity (n, %)	
Mild	1 (2.3%)
Moderate	8 (18.2%)
Severe	35 (79.5%)
PFO present (n, %)	23 (52.3%)

Table-2: Post-operative outcome

Characteristics	
Duration of intubation (days) mean ±SD	4.05±6.58
Extubation failure (n, %)	12 (27.3%)
CICU stays (days) mean ± SD	6.60±7.18
Hospital stay (days) mean±SD	12.05±7.74
Post-operative ionotropic score mean ±SD	33.27±71.13
Low cardiac output syndrome (LCOS) (n, %)	12 (27.3%)
Arrhythmia (n, %)	
Junction rhythm	7 (15.9%)
Heart block	3(6.8%)
Ventricular tachycardia	1(2.3%)
Others	1(2.3%)
Outcome (n, %)	
Discharged	39 (88.6%)
Expired	5 (11.3%)

Table-3: Comparison of results of two eras

	Initial 6 years (n=19)	**Last 6 years (n=25)**	**Statistical significance**
CPB time	155.79±69.61	118.20±50.97	p <0 .003
ACC time	117.42±75.55	86.40±36.06	p<0.019
Ionotropic score	29.16±28.59	36.80±91.70	p<0.046
Intubation duration	5.42±8.95	2.84±3.85	p<0.056
CICU stay	8.74±9.49	4.84±4.11	p<0.015
Hospital stay	14.05±8.90	10.48±6.38	p<0.046
Mortality	3 (15.7%)	2 (8%)	p<0.30

DISCUSSION

With improvements in surgical mortality and morbidity early primary surgical repair of ToF is the standard practice in the developed countries with some centres performing repair in neonatal age(10), with a reported mortality of 0-2%.[9] In developing countries, where late repair is the usual practice, reported mortality of ToF repair in infancy is as high as 5.7–14.2%.[11,12] Two stage operations have increased risk of complications such as distortion of the pulmonary arteries, suboptimal development of the pulmonary vasculature; shunt thrombosis, pulmonary vascular disease, end-organ dysfunction due to prolonged periods of cyanosis, right ventricular hypertrophy and diastolic dysfunction, leading to arrhythmias and sudden death later in life.[13,14] In Pakistan, like many other developing countries, late diagnosis, lack of medical facilities, surgical expertise, parental education, and financial constraints are the different factors which contribute towards late repair.

At our centre we started performing surgical repair of TOF under one year only in 2007. In the initial years, early surgical morbidity and mortality was very high but in the last six years we have improved results in mortality as well as morbidity. The mortality has decreased from 18.7 to 8%. Knott-Craig and colleagues reported a decrease in surgical mortality after primary repair of TOF in all ages from 11% before 1990 to 2.1% after 1990.[15] Although our mortality is still very high from standards worldwide, but it is comparable to what reported from developing countries, 5.7–14.2%.[11,12]

Our mean CPB time and ACC time were 133.52±62.41 and 98.66±58.62 respectively which are comparatively higher than what Egbe and colleagues have reported.[9] Our incidence of JET (15.9%) is higher than that reported by Anderson *et al* and Batra *et al*[16,17], while it is better than Khatami *et al* who reported JET in 21.9% in postoperative TOF repair.[18] Our CICU stay was comparable to that reported by other investigators: Hirsh *et al* reported a mean ICU stay of 9±8 days, Kolcz and Pizarro[19] reported a mean ICU stay of 7 days, and Tamesberger *et al*[20] reported mean CICU stay of 6

days. The intubation duration and hospital stay were slightly higher than that found by Egbe and colleagues.[9]

Prolonged CPB and ACC times are major risk factors for increase morbidity and mortality post congenital heart disease repair.[21] In the last six years our mean CPB time has reduced from 155.79±69.61 to 118.20±50.97 (p<0.003), aortic cross clamp time decreased from 117.42±75.55 to 86.40±36.06 (p<0.019) and our surgical mortality has gone down to 8% from 15.7% (p<0.30). This decrease in CPB and ACC times has probably resulted in improvement in our morbidity. Our surgical morbidity has decreased considerably in the last six years, so has the intubation duration (although statistically not significant (p<0.056), CICU stay (p<0.015) and hospital stay (p<0.046) have all improved. This reflects our learning curve with improved surgical skills, and perioperative care.

One of the main complications after relief of RVOT obstruction is the development of pulmonary regurgitation postoperatively, which can lead to progressive RV dilation, and if becomes severe, life-threatening arrhythmias and sudden death can ensue.[22] For this reason, patients undergoing TOF repair need to be followed for the remainder of their life. Children usually tolerate pulmonary regurgitation well during early postoperative period, but if PR increases in severity it can lead to severe consequences later in adult life as described earlier. In our study we followed these patients for up to one-year post TOF repair, 59.1% had mild PR in immediate postoperative period, at short term follow up majority 66% had mild to moderate PR, at mid-term follow up majority 52.9% had moderate to severe PR. These patients will require a long-term close follow up for progression of PR to enable timely intervention to prevent its complications.

Study limitations: Our study has few limitations; first due to lack of randomization and retrospective nature, this study is prone to bias. Secondly, small number of patients and low incidence of complications could undermine the accuracy of the statistical analysis of potential predictors of morbidity and mortality. Finally, our follow-up period is short.

CONCLUSION

TOF repair during infancy is safe procedure in expert hands with acceptable morbidity and mortality. In the last six years our surgical morbidity and mortality has improved considerably. Our results show that baseline saturation ≤75% is independent risk factors for LCOS and prolong intubation period. This should prompt Cardiac surgeons to undertake repairs in early infancy in severely hypoxic infants

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AUTHORS' CONTRIBUTION

MKYM: Data collection, literature search, manuscript writing. SA: Review of literature and manuscript. MM: Data collection and literature search. AA: Data collection. WA: Review of manuscript and proof reading. MAA: Designing, final approval and review of manuscript.

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