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Outcomes of Newborns with Tracheo-Esophageal Fistulas (Tef) in Combined Military Hospital, Peshawar

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ABSTRACT

Objectives: To determine the incidence of various outcomes in neonates with Tracheo-Esophageal Fistulas (TEF) after surgery and to evaluate the risk factors associated with mortality.

Study Design: Prospective cohort study.

Place and Duration of Study: Department of Pediatrics, Combined Military Hospital (CMH), Peshawar Pakistan, Jan 2023 to Aug 2024.

Methodology: This study was conducted after enrolling 31 neonates with TEF diagnosed via clinical, radiographic, and/or endoscopic findings. Neonates with fatal chromosomal anomalies incompatible with life, those who did not undergo surgical correction or were lost to follow-up were excluded. All patients underwent surgical correction of the defect and were managed post-operatively in the neonatal intensive care unit (NICU). Post-discharge, they were followed at regular intervals for one year to check for the development of complications.

Results: Of the 31 patients studied, most were males (n=18, 58.10%). The most common fistula seen was Type C, accounting for 25(80.60%) cases. Patent ductus arteriosus was the most common type of cardiac anomaly seen (n=5, 16.10%), and cardiac anomalies were more commonly seen in patients who died (p=0.01). Duration of mechanical ventilation was higher in patients who died: 69.00 (IQR: 29.00) hours versus 48.00 (IQR: 37.00) hours, (p=0.06). Pneumothorax (p<0.001) and sepsis (p<0.001) were more commonly seen in cases where patients died (n=5, 16.10%).

Conclusion: The presence of cardiac anomalies, and the occurrence of post-operative complications, particularly sepsis and pneumothorax, is associated with higher mortality.

Keywords: Neonates, Outcomes, Tracheo-Esophageal Fistulas.

How to Cite This Article: *Murtaza S, Shah SAH, Razzaq A, Ibrahim S, Ahmad S. Outcomes of Newborns with Tracheo-Esophageal Fistulas (Tef) in Combined Military Hospital, Peshawar. Pak Armed Forces Med J 2025; 76(Suppl-2): S460-S463. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-2.12754*

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INTRODUCTION

Tracheoesophageal fistula (TEF) is a congenital defect involving an abnormal connection between the trachea and esophagus, leading to significant health risks for neonates, including high morbidity and mortality, as despite advancements in surgery and neonatal care, prognosis remains difficult especially in low-resource settings.[1,2] TEF occurs in about 1 in 3,500 live births and requires precise timing for diagnosis and surgery to avoid complications such as aspiration pneumonia and severe respiratory distress.[3,4] The prognosis varies significantly, ranging from complete recovery to chronic complications or death.[4] Key factors influencing outcomes include the type and complexity of TEF, presence of other congenital anomalies, and promptness of medical intervention, where isolated TEF, with no additional anomalies, generally has a better outcome, while neonates with associated conditions like cardiac defects or chromosomal abnormalities face greater challenges.[5,6] Early diagnosis, whether before birth or immediately after, is critical for improving outcomes and recognizing symptoms such as excessive drooling, coughing, and respiratory distress can lead to timely surgery and better results.[5,6] Delayed diagnosis and intervention often result in complications like anastomotic leaks, strictures, recurrent fistulas, and respiratory issues.[7,8] Postoperative care plays a crucial role in recovery, with effective management of complications like infections and feeding issues being essential for favorable outcomes.[9,10] Multidisciplinary care teams, including neonatologists, pediatric surgeons, and specialized nurses, are vital to address the complex needs of these patients and this study aims to highlight factors affecting the prognosis of neonates with TEF. Improving understanding of these factors can enhance care quality, improve survival rates, and reduce the burden of TEF in Pakistan.

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Received: 02 Oct 2024; revision received: 02 Dec 2024; accepted: 06 Dec 2024

METHODOLOGY

This prospective cohort study was conducted in the Department of Paediatrics, Combined Military Hospital (CMH), Peshawar Pakistan. The study period spanned from January 2023 to August 2024 after obtaining ethics approval from Institutional Review Board vide letter (ERC). Consent was obtained from all participants, and the study was designed and executed in line with the Declaration of Helsinki and our own institutional ethical standards. The World Health Organisation (WHO) sample size calculator was used to calculate the sample size, keeping a confidence level (1-α) of 95%, absolute precision of (d) 0.05, and an anticipated population proportion (P) of 2.0%,[11] which were the percentages of patients with tracheo-esophageal fistulas who developed anastomotic leaks post-repair. The final study sample was composed of 31 patients who were diagnosed with TEF, who were enrolled through consecutive, non-random sampling.

Inclusion Criteria: All paediatric patients with a confirmed diagnosis of TEF through clinical, radiographic, and/or endoscopic findings were included.

Exclusion Criteria: Neonates with fatal chromosomal anomalies and other organ malformations incompatible with life, those who did not undergo surgical correction, such as extremely premature patients, and those lost to follow-up were excluded.

All data was collected prospectively using a structured data collection form. Variables recorded included demographic information such as gestational age at birth, birth weight, gender and mode of delivery, parameters related to clinical presentation such as timing of diagnosis and the presence of associated abnormalities. All patients underwent surgical correction of the TEF defect, and details were recorded, such as timing of surgical intervention and intraoperative findings, as well as postoperative management parameters, such as duration of mechanical ventilation, length of neonatal intensive care unit (NICU) stay, and the occurrence of complications. Neonates were followed up at regular intervals in the paediatric outpatient clinic for up to one-year post-discharge. Data was analyzed using the Statistical Package for the Social Sciences version 27.00. Mean±SD or median/interquartile range (IQR) were calculated for quantitative variables, specifically maternal age at birth, gestational age at birth, birth-weight, age at presentation, duration of mechanical ventilation, age at time of surgery, length of surgery, post-operative length of NICU stay, time to start of nasogastric (NG) feeding, and time to start of oral feeding. Qualitative variables, like gender, in-born or referred, mode of delivery, whether diagnosed antenatally or post-natally, antenatal findings/post-natal findings, findings on 2D echo, presence of associated dysmorphisms, mode of mechanical ventilation, type of surgery, type of fistula, post-operative complications and post-operative outcomes, were recorded in terms of frequency and percentage. Patients were divided into two groups based on whether death occurred or not. Qualitative data was compared between groups using the Chi Square test and Fischer Exact test, while quantitative variables were compared using the independent samples t test and Mann-Whitney U test. Normality was assessed using the Shapiro-Wilk test where a *p*-value of ≤0.05 was considered significant.

RESULTS

Our study sample comprised of 31 patients diagnosed with TEF. The median maternal age at the time of delivery was 29.00 (IQR: 6.00) years, with a median gestational age at the time of birth of 37.00 (IQR: 4.00) weeks. Males were more (n=18, 58.1%) and 12(38.70%) patients were delivered in-hospital, while the remaining 19(61.30%) were referred from other healthcare institutions. Vaginally delivered patients numbered 18(58.10%) while the remaining 13(41.90%) cases were delivered by Caesarean section. The median birthweight of this sample was 2063.00 (IQR: 381.00) g. Table-I shows detailed patient characteristics distributed according to the occurrence of death.

Table-I: Patient Characteristics According to Mortality (n=31)

Variable		Dead (n=5)	Alive (n=26)	*p*-value
Maternal age (years)		28.00 (IQR: 9.00)	30.00 (IQR: 6.00)	0.39
Gestational age at birth (weeks)		33.00 (IQR: 2.00)	37.00 (IQR: 4.00)	<0.001
Birthweight (g)		1913.00 (IQR: 66.00)	2140.50 (IQR: 393.00)	<0.001
Gender	Male	3(60.00%)	15(57.70%)	1.00
	Female	2(40.0%)	11(42.30%)	

Table-II displays the different disease characteristics of the patients at the time of initial presentation, where a total of 5(16.10%) patients had a patent ductus arteriosus (PDA), the most common cardiac anomaly seen, 2(6.50%) patients had an atrial septal defect (ASD), while 1(3.20%) patient had a ventricular septal defect (VSD). The most common fistula seen was Type C, accounting for 25(80.60%)

cases, 3(9.70%) patients had Type A fistulas, while Type B, D and E fistulas were seen in 1(3.20%) patient each.

Table-II: Disease Characteristics at the Time of Presentation According to Mortality (n=31)

Variable		Dead (n=5)	Alive (n=26)	*p*-value
Age at presentation (days)		15.00 (IQR: 8.00)	8.00 (IQR: 8.00)	0.14
Time to diagnosis (days)		21.00 (IQR: 11.00)	10.50 (IQR: 12.00)	0.16
Echocardiographic findings	Normal study	1(20.00%)	22(84.70%)	0.03
	PDA	3(60.00%)	2(7.70%)	
	ASD	1(20.00%)	1(3.80%)	
	VSD	-	1(3.80%)	
Clinical findings	Cough	2(40.00%)	16(61.50%)	0.63
	Fever	1(20.00%)	9(34.60%)	0.65
	Pneumonia	-	3(11.50%)	1.00
	Haemoptysis	1(20.00%)	1(3.80%)	0.30
	Dysphagia	1(20.00%)	4(15.40%)	1.00
Type of Fistula	Type A	1(20.00%)	2(7.70%)	1.00
	Type B	-	1(3.80%)	
	Type C	4(80.00%)	21(80.90%)	
	Type D	-	1(3.80%)	
	Type E	-	1(3.80%)	

**PDA: Patent ductus arteriosus, ASD: Atrial septal defect, VSD: Ventricular septal defect*

Table-III shows various characteristics of intervention conducted during the course of our study. The median age at the time of surgery was 4 (IQR: 7.00) months, median length of surgery was 75 (IQR: 66.00) minutes, median duration of mechanical ventilation was 55(78.00) hours, while the length of NICU stay was 8 (IQR: 8.00) days. The median time to nasogastric (NG) feeding was 6 (IQR: 3.00) days where a total of 10(32.30%) patients developed esophageal strictures and anastomotic leaks were seen in 7(22.60%) patients, 3(9.70%) patients developed pneumothorax, and 6(19.40%) patients had sepsis.

Table-III: Intervention Characteristics According to Mortality (n=31)

Variable		Dead (n=5)	Alive (n=26)	*p*-value
Age at surgery (days)		5.00 (IQR: 2.00)	4.00 (IQR: 4.00)	0.86
Length of surgery (minutes)		73.00 (IQR: 14.00)	82.00 (IQR: 41.00)	0.42
Duration of mechanical ventilation (hours)		69.00 (IQR: 29.00)	48.00 (IQR: 37.00)	0.06
Length of NICU stay (days)		5.00 (IQR: 10.00)	8.0 (IQR: 9.00)	0.62
Time to NG feeding (days)		6.00 (IQR: 3.00)	6.00 (IQR: 3.00)	0.62
Post-operative complications	Stricture formation	2(40.00%)	8(30.8%)	1.00
	Anastomotic leak	1(20.00%)	6(23.10%)	1.00
	Pneumothorax	3(60.00%)	-	<0.001
	Sepsis	5(100.00%)	1(3.80%)	<0.001

**NICU: Neaonatal Intensive Care Unit, NG: Nasogastric*

DISCUSSION

Our study evaluated the outcomes of 31 neonates diagnosed with various forms of TEF, with the results indicating that gestational age and birthweight, associated anomalies, and post-operative complications are critical determinants of survival in these patients. Our analysis showed that lower gestational age was associated with increased mortality, a finding that is in agreement with previous literature that typically correlates lower gestational age with poorer outcomes, particularly those born at <34 weeks of gestation, faced a higher risk for the development of complications, such as respiratory distress syndrome (p<0.00) and intraventricular haemorrhage (p=0.03), potentially predisposing patients to the occurrence of death, however, the study had a short-term follow-up and did not report on long-term mortality.[12] Increased mortality observed in premature infants with TEF may largely be attributed to the complications associated with prematurity itself, however, these infants are also at a higher risk of being born with low birth weight, which further elevates the risk of mortality in TEF patients, as demonstrated in our study. One researcher reported a proportional increase in mortality with decreasing birth weight in their cohort of patients with esophageal atresia/TEF[13] which was corroborated by another author, who identified a significant risk associated with birth weights below 2500 g (aHR 1.49, 95% CI, 1.02–2.21).[14] Notably, cardiac anomalies were common in our cohort which was significantly associated with increased mortality, similar to other studies reporting a frequency between 20% and 25%.[15,16] Additionally, studies have reported that the most commonly observed cardiac abnormalities in patients with TEF are PDA and ASD and incidence of mortality increases with the presence of these cardiac anomalies and rises further when multiple cardiac anomalies are present.16 Type C fistula was predominant in our study, consistent with another study reporting frequency of 94.60% cases.[15,17] Post-operative complications were a major determinant of mortality in our study and sepsis was observed in all patients who died while pneumothorax was also significantly associated with mortality, however, esophageal strictures and anastomotic leaks, although common, were not directly linked to increased mortality but may contribute to long-term morbidity and necessitate close follow-up. One author reported the frequency of complications including pneumothorax, anastomotic leakage and strictures, with frequencies of 38.90%, 18.10% and 63.70%,[8]

respectively, similar to our figures, while another study noted that early recurrence of fistula was seen in 12% cases, while anastomotic leaks were seen in 8%.[18]

LIMITATIONS OF STUDY

The limited sample size and the single-center nature of this study restrict the extent to which our findings can be generalized to a broader population. Moreover, the absence of long-term follow-up data further hinders our ability to fully comprehend the extended outcomes for these patients.

CONCLUSION

Key determinants of mortality identified in our research include gestational age at birth and birth-weight, the presence of associated cardiac anomalies, and the occurrence of post-operative complications, particularly sepsis and pneumothorax. The findings from our study emphasize the importance of adopting a multidisciplinary approach, along with the implementation of standardized management protocols, to optimize clinical outcomes for neonates affected by tracheoesophageal fistulas.

Conflict of Interest: None.
Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SM & SAHS: Data acquisition, data analysis, critical review, approval of the final version to be published.
AR & SI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.
SA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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