



ORIGINAL ARTICLE

Comparison of ligation versus preservation of azygous vein in primary repair of esophageal atresia with tracheoesophageal fistula in neonates.

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ABSTRACT... Objective: To compare frequency of anastomotic leak with ligation versus preservation of azygos vein in the primary repair of esophageal atresia (EA) with trachea-esophageal fistula (TEF) in neonates. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Pediatric Surgery, Pakistan Institute of Medical Sciences, Islamabad. **Period:** October 2019 to September 2020. **Material & Methods:** This study involved 180 neonates (1-28 days of life) of both genders undergoing primary repair of EA with TEF and divided in azygous vein ligation surgery and azygous vein preservation surgery. Outcome variable was frequency of post-operative anastomotic leak. **Results:** In a total of 180 neonates, mean age was 6.75 ± 6.39 days. Majority ($n=130$, 72.2%) of the patients were aged ≤ 7 days. There were 107 (59.4%) male and 73 (40.6%) female neonates. The frequency of anastomotic leak was significantly lower in Azygous vein preservation group (6.7% vs. 20.0%; $p=0.009$) as compared to azygous vein ligation group. **Conclusion:** Preservation of azygous vein was associated with significantly lower frequency of post-operative anastomotic leak among neonates undergoing primary repair of EA with TEF.

Key words: Anastomotic Leak, Azygous Vein Ligation, Esophageal Atresia, Tracheoesophageal Fistula.

INTRODUCTION

Esophageal atresia (EA) and tracheo-esophageal fistula (TEF) are one of major congenital anomalies that affect 1:3500 live births.¹ About one-third of these children are born early.² Currently the research is mainly focused on understanding the possible etiology of these birth defects. Advancements in genotyping technology and human genetic variation will surely improve the understanding of these defect with better clinical counseling on etiologic factors.¹

The diagnosis of EA is made usually during the first twenty four hours of life but may be made either antenatally or may be delayed. Till now the esophagus no ideal replacement and for patients with long-gap EA, the optimal surgical treatment is still controversial.² The surgical management of neonates having EA with or without TEF is

considered as one of the major triumphs of pediatric surgery in the 21st century.³ Depending on the criterion used incidence of anastomotic leakage varies from 4 to 36%.⁴ Anastomotic leak occurred in 6% (3/46) in with azygous vein preservation while 20% (10/50) with azygous vein ligation for EA repair. The difference was found to be significant ($P<0.05$). Authors concluded that preserving azygous vein prevents early postoperative edema of esophageal anastomosis as venous drainage is maintained and thus may act as an additional protective factor against anastomotic leakage.⁵ One more study found that the frequency of anastomotic leak was 20% with azygous vein ligation while 12.3% with preservation of azygous vein although the difference was insignificant ($P>0.05$).⁶

Literature is evident that EA repair with preservation

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of azygous vein is associated with less anastomotic leak as compared to azygous vein ligation. But there also exists controversy which fallouts that often surgeons ligate the azygous vein during surgery.^{7,8} So through this study, we wanted to confirm that if azygous vein preservation is beneficial in form of less anastomotic leak, then in future we may be able to implement the method to preserved azygous vein instead of ligation. Moreover, this study involved a relatively large sample size as previous studies were conducted on small sample size. Furthermore, through this study we wanted to get local evidence which may help us in future to implement the use of azygous vein preservation instead of ligation which is thought to decrease morbidity and mortality associated with more anastomotic leak. This study was done to compare the anastomotic leak with ligation versus preservation of azygous vein in primary repair of esophageal atresia (EA) with TEF in neonates.

MATERIAL & METHODS

This randomized controlled trial was performed at Department of Pediatric Surgery, "Pakistan Institute of Medical Sciences (PIMS)", Islamabad from October 2019 to September 2020. Sample size of 180 patients (90 in each group) was calculated taking 80% power of test, 5% significance level and taking expected percentage of anastomotic leak to be 20% vs. 6%⁵ with and without ligation of azygous vein in children with EA+TEF. Non-probability, consecutive sampling technique was used. Neonates of age 1-28 days of either gender presenting with EA with TEF were included in the study. Neonates having long gap EA with or without TEF, where the primary esophageal anastomosis was not possible (on clinical examination) and neonates with abnormal clotting profile (PT >20sec, aPTT >15sec) were excluded.

Informed consent was obtained from parents. Approval from Institutional Ethical Committee was acquired (letter dated: 01-10-2019). Demographic profile (name, age, gender, address and contact) were also noted. Then they were randomly divided in two equal groups by using lottery method. In Group A, neonates underwent

primary repair with ligation and division of azygous vein. In group B, neonates underwent primary repair with preservation of azygous vein. All surgeries were done under general anesthesia by a single surgical team. Feeding through trans-anastomotic tube was started after 24 hours of surgery in all patients. All the patients received same pre and postoperative treatment. Oral feed was started following a water soluble contrast esophagography on 5th postoperative day using diluted gastrograffin. Then neonates were shifted to ward and followed-up there till 7th post-operative day for assessment of anastomotic leak. All this information was recorded in pre-designed proforma.

Data was analyzed using "Statistical Package for Social Sciences (SPSS)" version 26.00. Age was presented by mean±SD. Qualitative data were described by frequency and percentage. Stratification was done for study variables and post-stratification chi-square test was employed taking p value ≤0.05 as statistically significant.

RESULTS

In a total of 180 neonates, the mean age was 6.75±6.39 days ranging 1 to 28 days. Majority (n=130, 72.2%) of the patients were aged ≤7 days. There were 107 (59.4%) male and 73 (40.6%) female patients in the study group. Both the groups were comparable in terms of mean age (p=0.972), and age (p=0.506) and gender (p=0.879) groups as shown in Table-I.

The frequency of anastomotic leak was significantly lower in Azygous vein preservation group (6.7% vs. 20.0%; p=0.009) as compared to azygous vein ligation group (Table-II).

Anastomotic leak across study groups with respect to age and gender is shown in Table-III. It was found that anastomotic leak was significantly more among children aged less than 7 days among ligation of vein group (19.4% vs. 6.3%, p=0.027) while all other study variables did not have any significant association with anastomotic leak.

Characteristics	Study Sample n=180	Ligation of Azygous Vein (n=90)	Preservation of Azygous Vein (n=90)	P-Value
Age (days)	6.75±6.39	6.73±6.28	6.77±6.54	0.972
• ≤7 days	130 (72.2%)	67 (74.4%)	63 (70.0%)	0.506
• >7 days	50 (27.8%)	23 (25.6%)	27 (30.0%)	
Gender				
• Male	107 (59.4%)	54 (60.0%)	53 (58.9%)	0.879
• Female	73 (40.6%)	36 (40.0%)	37 (41.1%)	

Table-I. Baseline characteristics of study cases (n=180)

Anastomotic Leak	Study Group		Total	P-Value
	Ligation of vein (n=90)	Preservation of vein (n=90)		
Yes (n=24)	18 20.0%	6 6.7%	24 13.3%	0.009
No (n=156)	72 80.0%	84 93.3%	156 86.7%	

Table-II. Distribution of Anastomotic leak across Study Groups (n=180)

Study Variables		Anastomotic Leak	Study Group		P-Value
			Ligation of vein (n=90)	Preservation of vein (n=90)	
Age Groups	≤7 days	Yes	13 (19.4%)	4 (6.3%)	0.027
		No	54 (80.6%)	59 (93.7%)	
	>7 days	Yes	5 (21.7%)	2 (7.4%)	0.145
		No	18 (78.3%)	25 (92.6%)	
Gender	Male	Yes	11 (20.4%)	4 (7.5%)	0.056
		No	43 (79.6%)	49 (92.5%)	
	Female	Yes	7 (19.4%)	2 (5.4%)	0.068
		No	29 (80.6%)	35 (94.6%)	

Table-III. Anastomotic leak across study groups with respect to age and gender (n=180)

DISCUSSION

In the present study, majority (72.2%) of the patients were aged ≤7 days. Anwar-ul-Haq et al. (2009) in a similar local study also observed higher proportion of this age group (77%) among neonates presenting with EA with and without fistula at Pakistan Institute of Medical Sciences (PIMS), Islamabad.⁷ There were 107 (59.4%) male and 73 (40.6%) female patients in the study group giving a male to female ratio of 3:2. A similar male predominance among patients of EA has been reported by Rashid et al. in 2012 (61.2% vs. 38.8%) in Indian⁶ and Anwar-ul-Haq et al. in 2009 (66.3% vs. 33.7%) in Pakistani population.⁷ Much higher male predominance (5.6:1) has been reported by Gupta et al. in Indian population.⁴

Present research claimed that EA repair with preservation of azygous vein was associated with

less anastomotic leak as compared to azygous vein ligation. The frequency of anastomotic leak was significantly lower in Azygous vein preservation group (6.7% vs. 20.0%; $p=0.009$) as compared to azygous vein ligation group. Similar difference was observed across all age and gender groups. However existing literature shows controversial results and lack of local published results necessitated the present study. Our results are comparable to those of Sharma et al. who also observed significantly lower frequency of post-operative anastomotic leak with preservation of azygous vein (6.0% vs. 20.0%; $p<0.05$).³ A study conducted by Cui et al showed that anastomotic leak was significantly lower with preservation of azygos vein as compared to ligation ($p=<0.05$). They also concluded that preservation of azygos vein had lower incidence of esophageal stricture after one year of follow up ($p=<0.05$).⁸ In

another study anastomotic leakage was 18.2% in azygos preservation group as compared to azygos ligation group in which the percentage of anastomotic leakage was 34.1%.⁹ In a study conducted on 60 full term neonates by Mohantay et al no significant difference was found in terms of anastomotic leakage between azygos preservation and ligation.¹⁰ This difference in result may be due to small sample size in this study. A study conducted by Nisar et al at the children's hospital PIMS Islamabad also concluded that there is no difference in azygos vein ligation vs preservation in terms of post-operative complications like leakage, sepsis and pneumonia.¹¹ A recent meta-analysis by Kainth D et al concluded that surgical repair to EA adopting preservation of azygos vein resulted in significant reduction in post-operative chest infection.¹² Upadhyaya VD et al found that preservation of azygos vein maintained normal venous drainage of mediastinum so resulted in reduction in post-operative chest congestion and pneumonia.¹³ Some other researchers have also shown that although, preservation of zygus vein restored normal mediastinal anatomy but resulted in relatively increased surgery time and did not impart beneficial outcomes in terms of mortality or post-surgical complications.^{14,15}

Thus the hypothesis established at the start of study is well proved and preservation of azygos vein significantly lowers the frequency of post-operative anastomotic leak (6.7% vs. 20.0%; $p=0.009$) among neonates undergoing primary repair of EA with TEF. In the light of results of the present study, it can be advocated that in future practice azygos vein should be saved during primary repair of EA so as to minimize the risk of post-operative anastomotic leak with its associated morbidity and mortality.¹⁶⁻¹⁸

Limitations of the Study: The results of the present study are reliable due to strict exclusion criteria and stratification of effect modifiers. However, there is a limitation to the present study and that is its limited sample size of 180 patients which produced insignificant difference upon stratification of results. Therefore there is need to repeat this trial over larger sample size to further confirm the results.

CONCLUSION

Preservation of azygos vein was associated with significantly lower frequency of post-operative anastomotic leak among neonates undergoing primary repair of esophageal atresia with tracheoesophageal fistula.






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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Hamayun Anwar	Methodology, Discussion.	
3	Abdul Hameed Khan	Study concept, Data Analysis, Proof reading.	
4	Mohammed Abdulmomen Abdullah Saif	Data collection, Literature review.	
5	Ali Raza Chaudhry	Data collection, Literature review.	
6	Ramsha Syed	Data interpretation, References	