

## The Some Predictive Factors for Survival of Newborns with Esophageal Atresia

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### Abstract

#### Background

The esophageal atresia (EA) is the most common esophageal congenital anomaly. The aim of this study was to evaluate the predictive factors in the survival of newborns with esophageal atresia.

#### Materials and Methods

This was a descriptive-analytic cross-sectional study performed on newborns with esophageal atresia who were admitted at Bahrami children's hospital, Tehran-Iran, during 7 years (2009-2015). The patient's information was collected from their medical records and recorded in a checklist. The variables of the checklist included: age, sex, gestational age, birth weight, congenital anomalies, duration of mechanical ventilation, duration of hospitalization, respiratory distress syndrome (RDS), and age at surgery, complications, and cause of death. Then, the relationship between different variables was evaluated with mortality and morbidity and the factors that had the greatest impact on patients' prognosis were identified.

**Results:** The study included 95 neonates with EA. Fifty-three (55.8%) were male. The most common anomalies were cardiac (38.9%), renal (15.8%), and skeletal (9.5%). The most common postoperative complication was pneumothorax (31.6%), pneumonia (25%), and stenosis at the site of anastomosis (21.1%). In this study, 15 children died (mortality rate 15.7%), and the most common cause was sepsis. There was a significant relationship between birth weight and death, pneumothorax ( $P=0.008$ , and  $P=0.037$ , respectively). There was no significant relationship between gestational age and mortality ( $P>0.05$ ). There was a significant relationship between major cardiac anomalies and duration of mechanical ventilation and mortality ( $P=0.043$ , and  $P<0.001$ , respectively).

#### Conclusion

This study showed that neonates with esophageal atresia, low birth weight, major cardiac anomalies and the need for prolonged mechanical ventilation are poor prognosis predictor factors.

**Key Words:** Cardiac anomalies, Esophageal atresia, Low birth weight, Newborn.

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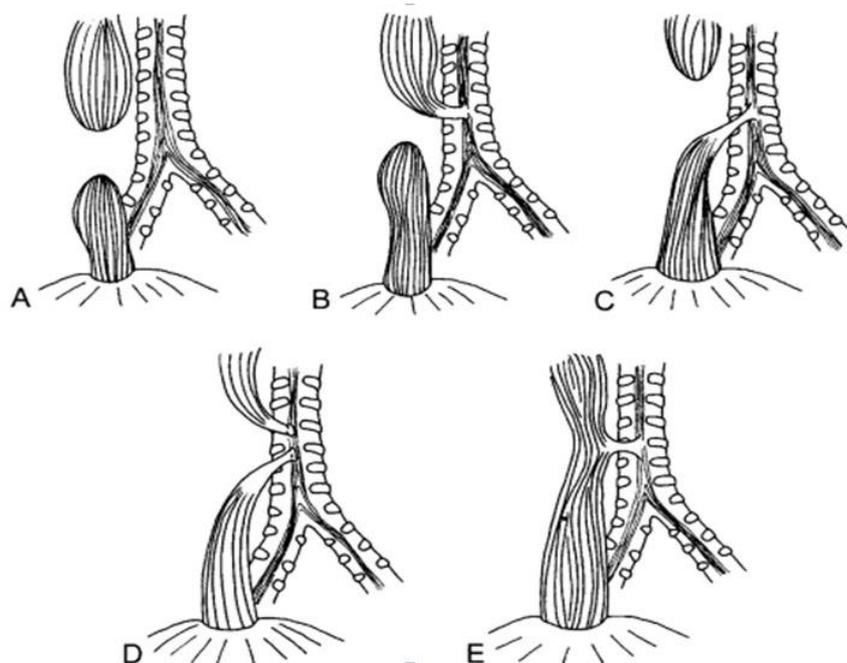
## 1- INTRODUCTION

Esophageal atresia (EA) is the most common esophageal congenital anomaly with an incidence of 1 in 2,400–4,500 live births (1). The classification of the esophageal atresia is based on the location of the atresia, and the presence of any fistula between the trachea and the esophagus (**Figure.1**) (2). About half of these neonates have other anomalies including cardiovascular (35%), genitourinary (24%), gastrointestinal (24%), and vertebral/skeletal (13%), and neurological (10%) anomalies (3). These anomalies affect the treatment and survival of these patients (4). These congenital anomalies are termed "VACTERL" (vertebral, anorectal, cardiac, tracheal, esophageal, renal, and limb) (2, 4). EA has been associated with high mortality and morbidity rate, but today, due to the advances in surgical techniques, nutritional support and intensive care, the survival of affected neonates has improved (5). So that for the past 10 years, the survival rate of these neonates has been about 92.0% (4, 6, 7). Different classification scoring

systems such as Spitz, Waterston, and Matthew have been used for defining the probability of survival in neonates with EA (8- 11). The Spitz's classification of risks associated with survival in these neonates is depicted below (8):

1. Group I Birth weight over 1,500 g with no major cardiac anomaly.
2. Group II Birth weight less than 1,500 g or major cardiac anomaly.
3. Group III Birth weight less than 1,500 g PLUS major cardiac anomaly.

The Montreal classification system considers weight as an important predictive factor (12). In previous studies different factors were considered as predictive of survival in neonates with esophageal atresia such as prematurity, low birth weight, respiratory failure, postoperative sepsis, pneumothorax, and septic shock (5). The predictive factors of survival have changed according to the time and institution (5, 7). So we aimed to evaluate the predictive factors in the survival of newborns with esophageal atresia.



**Fig.1:** The classification of the esophageal atresia.

Type A: without a fistula (8%), type B: with proximal fistula (1%), type C: with a distal fistula (86%), type D: with fistula on both sides (1%), and type E or H-type: without esophageal atresia (4%) (2).

## 2- MATERIALS AND METHODS

### 2-1. Study design

This retrospective study was conducted in Bahrami children's hospital (affiliated to Tehran University of Medical Sciences) between July 2009 and July 2015. Medical records of all neonates with EA were reviewed. The checklist was designed based on previous studies, which include some variables affecting mortality and morbidity of the infant with esophageal atresia. The checklist was completed for each patient by the researchers, based on the information from their medical records in the hospital archive, which included: age, gender, gestational age, birth weight, congenital anomalies, duration of mechanical ventilation, duration of hospitalization, respiratory distress syndrome (RDS), surfactant administration, age at surgery, type of surgery, complications (such as pneumonia, anastomotic leakage, stenosis at the site of anastomosis, infection and pneumothorax), and the cause of death. The exclusion criteria were the incomplete medical records.

### 2-2. Ethical Considerations

The study has been approved by the local ethics committee of Tehran University of Medical Sciences (Approved Number: IR.TUMS.REC.1394.1762).

### 2-3. Statistical methods

The data was analyzed using SPSS software (SPSS Inc., Chicago, IL, USA), version 24.0. The descriptive data were reported using descriptive statistics including standard deviation, frequency,

and relative frequency. Chi-square test was used to determine the relationship between qualitative variables and survival and postoperative complications. In the case of the normal distribution the student t-test was used to determine the relationship between qualitative variables and survival and postoperative complications, and in the case of the non-normality distribution the Mann-Whitney test was used. P-value less than 0.05 was considered statistically significant.

## 3- RESULTS

Ninety-five patients were enrolled. Forty-two (44.2%) were female and fifty seven (55.8%) male. Their mean weight was  $2612 \pm 599.5$  gr (range: 1000-3980 gr). The mean gestational age was  $36.86 \pm 2.44$  weeks (range: 27-41 weeks). The baseline characteristics were summarized in **Table.1 and 2**. The most common associated congenital anomalies were cardiac in 38.9% (n=37), renal in 15.8% (n=15), and skeletal in 9.5% (n=9). The frequency of esophageal atresia types was type C 80% (n=76), type A 18.9% (n=18), and H-type 1.1% (n=1), according to the Gross classification. Surgery was performed in ninety-three patients. Postoperative complications occurred in 55 (59%). The most common complications were pneumothorax (31.6%, n=30), pneumonia (25%, n=24), anastomotic stricture (21.1%, n=20), anastomotic leakage (5.3%, n=5), and infection (4.2%, n=4). Fifteen infants (15.7%) died. The most common cause of death was sepsis (26.6%, n=4). **Table.3** indicates the causes of death.

**Table-1:** Baseline characteristics of the infants with esophageal atresia (n=95).

Variables	Mean $\pm$ Standard deviation	Min-Max
Gestational age (week)	36.8 $\pm$ 2.4	27-41
Birth weight (gr)	2612.2 $\pm$ 599.5	1000-3980
Age at operation (days)	4.6 $\pm$ 2.3	1-12
Duration of Ventilation (days)	4.2 $\pm$ 5.9	1-30
Hospital admission (days)	25.3 $\pm$ 16.7	1-93

**Table-2:** Baseline characteristics and their impact on Survival (n=95).

Independent factor		Total Case (%)	Survival
Age at presentation	1	91 (95.8%)	76 (83%)
	2	2 (2.1%)	2 (100%)
	3	1 (1.1%)	1 (100%)
	4	0 (0.00%)	---
	5	1 (1.1%)	1(100%)
Age at operation days	1-5 days	65 (68.4%)	56 (86%)
	6-10 day	25 (26.3%)	22 (88%)
	11-15 day	3 (3.2%)	2 (66%)
	No surgery	2 (2.1%)	0 (00%)
Gestational Age	≥37 weeks	67 (70.5%)	63 (94%)
	28-36 weeks	26 (27.4%)	16 (61%)
	<28 weeks	2 (2.1%)	1 (50%)
Weight	≥2500	58 (61.1%)	53 (91.4%)
	1500-2499	34 (35.8%)	26 (76.5%)
	1000-1499	3 (3.2%)	1 (33.3%)
Gender	Mail	53 (55.8%)	44 (83%)
	Female	42 (42.2%)	36 (85%)
Anomaly	Cardiac	37 (38.9%)	30 (75%)
	Kidney	15 (15.8%)	13 (86%)
	Skeletal	9 (9.5%)	9 (100%)
<b>Group High Risk</b>			
Waterson Classification (B)	A	40 (42.1%)	38 (95%)
	B	37 (38.9%)	32 (86.5%)
	C	18 (18.9%)	10 (55.6%)
Spitz Classification (9)	A	69 (72.6%)	63 (91.3%)
	B	24 (25.2%)	17 (70.8%)
	C	2 (2.1%)	0 (0.00%)
Type of Atresia	A	18 (18.9%)	14 (77%)
	B	0 (0.00%)	--
	C	76 (80%)	65(85%)
	D	0 (0.00%)	--
	E (or H type)	1 (1.1%)	1 (100%)
Duration of Mechanical Ventilation	1-5 days	78 (82.1%)	70 (89.7%)
	6-10 days	8 (8.4%)	8 (100%)
	11-15 days	2 (2.1%)	1 (50%)
	16-20 days	4 (4.2%)	0 (0.00%)
	21 25 days	1 (1.1%)	1 (100%)
	26-30 days	2 (2.1%)	0 (0.00%)
Duration of Hospitalization	1-20 days	51 (53.7%)	42 (82%)
	21-40 days	30 (31.6%)	28 (93%)
	41-60 days	11 (11.6%)	8 (72%)
	61-80 days	1 (1.1%)	0 (00%)
	81-100 days	2 (2.1%)	0 (100%)

**Table-3:** Frequency and causes of death in the infants with esophageal atresia.

Death cause	Frequency	With cardiac anomaly
Sepsis	4(26.6%)	0
Multiple anomalies syndrome	4 (26.6%)	1 <sup>§</sup>
Pneumonia	3 (20.0%)	2 <sup>¥</sup>
Cardiac anomaly	2 (13.3%)	2 <sup>£</sup>
Apnea	1 (6.6%)	0
Surgery	1 (6.6%)	0
Total	15	5

§. Cardiomegaly. ¥. Tetralogy of Fallot, Pulmonary hypertension. £. Left ventricle hypoplasia, Tricuspid atresia.

There was a significant correlation between birth weight and death ( $P=0.008$ ); so that the mortality rate was higher in the low birth weight neonates. There was a significant relationship between duration of mechanical ventilation and mortality, pneumonia, pneumothorax and leak from the site of anastomosis ( $P=0.000$ ,  $P=0.016$ ,  $P=0.013$ , and  $P=0.013$ , respectively). Neonates with prolonged mechanical ventilation had a higher rate of mortality ( $P<0.001$ ). There was a significant correlation between syndromic multiple anomalies and surgical wound infection with mortality ( $P=0.005$ , and  $P=0.04$ , respectively). There was a significant difference between major cardiac anomalies and the type of them with mortality ( $P=0.03$ , and  $P=0.043$ , respectively), but there was no significant relationship between renal and skeletal

anomaly with mortality and postoperative complications ( $P>0.05$ ). There was no significant relationship between neonatal gender, mortality and complications after surgery ( $P>0.05$ ). No significant correlation was found between gestational age, RDS, and the type of esophageal atresia with mortality and complications after surgery ( $P=0.06$ ,  $P>0.05$ , and  $P>0.05$ , respectively). There was a significant relationship between gestational age and duration of the mechanical ventilation ( $P=0.003$ ). The birth weight had a significant correlation with pneumothorax ( $P=0.037$ ). So that low birth weight infants were more likely to have a pneumothorax. There was a significant relationship between gestational age and pneumonia ( $P=0.04$ ). **Table.4** compares the various differences among the patients who died and survived.

**Table-4:** Comparison of different factors between patients who died and survived.

Independent factor	Dead	Survived	P-value
Birth weight (g)	2257.3±578.2	2678.7±583.1	0.01
Duration of Mechanical Ventilation (days)	11±11	2.9±3.1	0.01
Hospitalization days	26.7±20.3	25±16	0.70
Gestational age	35.2±3.3	37.1±2.1	0.06
Gender			
Female	7(46.7%)	35(43.8%)	0.80
Male	8(53.3%)	45(56.3%)	

#### 4- DISCUSSION

Esophageal atresia is the most common congenital anomaly of the esophagus and can lead to high mortality and morbidity. The presence of other

associated anomalies may increase the frequency of mortality and morbidity. Different classifications are used for evaluation of the predictive factors of survival. According to our results, low

birth weight, major cardiac anomalies, long duration of mechanical ventilation, syndromic multiple anomalies and surgical wound infection were independent predictive factors for mortality. In the present study, like most previous studies, most patients were male (M/F=1.3/1) (7, 13- 18). The mortality rate in our study was about 15.8% and sepsis and multiple anomalies were the most common causes of death. The mortality rates have been reported differently (5%-56%) in various studies (6, 7, 13-23). These differences can be related to age on the presentation, delay in diagnosis and occurrence of complications like aspiration, pneumonia, and sepsis, transportation problems leading to hypothermia or hypoglycemia. In this study, duration of mechanical ventilation was significantly longer in newborns with esophageal atresia. Similar to our results, Sulkowski et al.'s found that birth weight, congenital cardiac disease, genetic anomalies, and preoperative mechanical ventilation as independent predictive factors for mortality (20). In this study, the cardiac anomalies were the most common(20). Wang and coworkers depicted a mortality rate in the EA patients of 9% (8). In this study, birth weight, operation on the first day of birth, and ventricular septal defect (VSD) were independent predictive factors for mortality (8). Young et al., suggested that the mortality rate was affected by life-threatening anomalies and postoperative complications including tracheomalacia/stenosis with dying spell (13). Tandon et al. showed that the life-threatening anomalies (especially cardiac), sever pneumonitis, sepsis, the presence of a long gap, and major leaks from the anastomotic site have a significant role in increasing mortality rate (14). Kumar and Ojha indicated severe bilateral pneumonitis, severe congenital anomalies (especially cardiac and genitourinary), prematurity, and hypothermia are poor prognosis predictive factors. (15); unlike

our study, in Kumar and Ojha's study, birth weight had no significant effect on the outcome (15). In the study of Engum et al., the most common cause of death were cardiac anomalies, fatal sleep apnea, renal failure, pulmonary failure, and trisomy (21). Lacher et al., like in our study, showed that birth weight less than 2500 g was survival predictor (22). Osia et al., suggested that congenital anomalies could lead to increased mortality rate in these patients (16). Goodarzi et al., showed that sepsis, aspiration pneumonia, prematurity, low birth weight and sever congenital heart disease were independent etiology of death (18). Ammar et al., indicated that prematurity, low birth weight, cardiac anomaly, delayed in diagnosis were poor prognosis predictive factors (17). Davari and colleagues showed that the mortality rate depends on the presence of cardiac anomalies, surgical delay, low birth weight, and prematurity (23). In our study, unlike Davari's (23), and Ammar et al.'s study (17), surgical delay and prematurity had no significant effect on the mortality rate. Shina et al. on the contrary, showed that birth weight, cardiac anomalies and duration of mechanical ventilation had no significant effect on survival (24). **Table.5** has compared our results with other studies. Our survival rate based on the Waterson classification (11) was 95% for class A, 86.5% for class B, and 55.6% for class C, while according to the Spitz classification (10), our survival rate was 91.3% for class A, 70.8% for class B, and 0.00% for class C. In the study, there were 28 (29%) premature neonates with gestational age less than 37 weeks. Of these, only 5 (17%) infants had RDS. There was no significant relationship between RDS and poor prognosis. Li et al. showed that low birth weight, anastomotic leak, respiratory failure, postoperative sepsis were the independent risk factor for poor outcomes (6). Templeton et al. and Li et al., showed that severe RDS leads to poor prognosis in patients with atresia. (25,

6). This finding is contrary to ours. This difference seems to be due to the fact that most patients with esophageal atresia were referred to our center from other hospitals. In case of severe RDS and instability of the infant's clinical condition, they could

not been referred to our hospital. Therefore, our results regarding RDS and its effect on the prognosis of neonatal with esophageal atresia are not meaningful or significant.

**Table-5:** Comparison of the recent study with results of similar studies (13-16).

Variables	Present	Osia et al. (16)	Yang et al. (13)	Tandon et al. (14)	Kumar et al. (15)
Total Case	95	37	15	127	69
Male/Female	1.3/1	1.6/1	1.1/1	1.9/1	1.8/1
Average birth weight (gr)	2612	2601	2491	-	2250
Gestational Age (week)	36.86	37.2	37	-	-
Congenital Anomalies	Cardiac (38.9%), Genitourinary (15.8%), Skeletal (9.5%).	Cardiac (10.8%) Genitourinary (5.4%).	Cardiac (53.3%), Respiratory (33.3%), Head & Neck (25%), Gastrointestinal (13.3%), Skeletal (16.7%) Genitourinary (6.7%).	Cardiac (13.3%), Gastrointestinal (11.8%), Vertebral & Nervous System (6.2%), Musculoskeletal (4.7%), Head & Neck (1.5%), Genitourinary (1.5%), Respiratory (1.5%), Cleft Lip (0.8%).	Cardiac (4.3%), Genitourinary (1.4%), Anorectal (4.3%).
Survival rate	84.3%	70.3%	53.3%	80%	51.2%
Most Common Type of Atresia	C (80%)	C 77.5%	C (80%)	C (92%)	-

## 5- CONCLUSION

Based on the results, in infants with esophageal atresia, birth weight, major cardiac malformations, duration of mechanical ventilation, syndromic multiple anomalies and surgical wound infection can be the predictive factors for survival.

**6- CONFLICT OF INTEREST:** None.

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