

# Associated Congenital Anomalies with Esophageal Atresia and their Impact on Survival in an Indian Scenario

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## ABSTRACT

**Introduction:** Congenital anomalies associated with the esophageal atresia may also lead to mortality and morbidity. Study was aimed to find out the role of associated congenital anomalies in the survival of Esophageal atresia in an Indian tertiary health centre.

**Material and methods:** In a prospective study from february 2008 to february 2016, 127 neonates with EA were admitted with age ranging from hours to 13 days. Diagnosis of associated congenital anomaly was done on the basis of physical examination and supported with investigations. Waterston prognostic criteria were used for survival.

**Results:** Associated congenital anomalies were present in 46 (36%) patients with VACTERL association in 6 (5%) cases. The survival was 49% in patients with associated anomalies and was 78% ( $p < 0.001$ ) in patients free from any other congenital anomalies.

**Conclusion:** In developing countries delayed diagnosis of congenital anomalies, poor transport facilities and delayed referral and lack of advanced neonatological setup leads to increased morbidity and mortality.

**Keywords:** Congenital Anomalies, Esophageal Atresia

## INTRODUCTION

Esophageal atresia is a common congenital disorder, its incidence ranging between 1/4000 to 1/5000. EA and TEF are life-threatening malformations of generally undefined cause. Previous reports of familial cases suggest a genetic contribution. The pattern of inheritance appears non-Mendelian, i.e., multifactorial. Individuals with EA/TEF often have other malformations and medical problems. EA results from the unsuccessful separation of the primitive foregut in to the ventral respiratory and dorsal digestive tract; this process is usually completed by the eight week of gestation. Associated congenital anomalies are present in nearly 50% of cases of EA<sup>1,2</sup> and responsible for morbidity and mortality. Recent improvements in surgical, neonatal care and safe anesthesia have remarkably improved the survival rate in the absence of associated anomalies. Study was done with the aim to know the role of associated congenital anomalies in the survival of Esophageal atresia in an Indian tertiary health centre.

## MATERIAL AND METHODS

From February 2008 to february 2016 a total number of 127 neonates were admitted with the diagnosis of EA (inform consent was taken from the patients parents and clearance from ethical committee). Preoperative assessment of gap was done with Plain X-ray chest (PA and lateral view) with No. 8 Fr Red Rubber catheter. Diagnosis of associated congenital anomaly was done on the basis of careful systemic and local

examination, radiological and sonological examination. Data collected included age at the time of admission, gestational age, birth weight, sex, home delivery /hospital delivery, associated congenital anomalies, respiratory status, and their impact on survival. Waterston prognostic criteria were used for survival. We defined a survival as an infant who leaves hospital able to take feeds well. The standard approach to EA was directed toward primary repair in all cases whenever possible except in cases of long gap, very low general condition or associated major gastrointestinal anomalies. Primary repair was done with retropleural approach with or without Azygos ligation, retropleural drainage and transanastomotic stenting.

## STATISTICAL ANALYSIS

Chi-square test and student's t- test was done for statistical analysis with the help of SPSS version 21.

## RESULTS

In our study of 127 cases of EA (figure-1), only 46 (36%) were admitted within 24 hours and 47 (37%) were admitted after 48hours with the most delayed admission was at age 13 days. 84 (66%) were males and 43 (34%) were females. 88 (69%) were full terms and 39 (31%) preterm. Weight ranged from 1.34 kg to 4.05 kg with a median weight of 2.50 kg. 60 (47%) were having weight >2.5 kg. Hospital based deliveries were in 66 (52%). Only 12 (9%) were having no respiratory distress at the time of admission, 44 (35%) were having mild, 58 (46%) having moderate and 13 (10%) were having severe respiratory distress. EA with distal TEF were the commonest type, 117 (92%) of cases, pure EA in 9 (7%) of cases and only one case of EA with proximal and distal fistula was present in the study. Associated congenital anomalies were present in 46 (36%) patients as given in table no 1. VACTERL association was present in 6 cases as given in table-2. The commonest associated anomaly was congenital heart disease (based upon preoperative clinical evaluation + post-operative echo-cardiogram) found in 17 (13%) cases.

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Rt aortic arch was present in 4 (3%) cases detected at the time of thoracotomy. Amongst 88 survived cases ECHO was done at the time of discharge. Six cases had congenital heart disease (VSD in 3 cases, ASD+VSD, PDA and Tetralogy of Fallot in one case each). The survival rate in EA was low (49 %) as compared to those free from any other congenital anomaly (78%) Survival rate among the cases of EA with congenital heart disease was 33% (p<0.001). EA with GI anomalies had mortality in 4 cases out of 39 (10%). Amongst VACTERL association no patient could survive either pre-operatively or post-operatively. Survival as per Waterston criteria was 100% in group A, 83% in group B and 22% in group C.

**DISCUSSION**

EA is reported to be associated with cardiovascular<sup>3,4</sup> gastrointestinal,<sup>5</sup> vertebral,<sup>6</sup> costal,<sup>7</sup> and urogenital anomalies.<sup>8</sup> The VACTERL association has been related to a high risk of mortality in patients with EA,<sup>9</sup> suggesting that the severity of the phenotypic presentation contributes to a significantly worst outcome. The development of EA and associated anomalies seems to be related to the malformation and ectopic location of the notochord. Many teratogenic events induce a global decrease in the proliferation of precursor cells in the perinotochordal mesenchyme. The resultant paucity of mesenchyme between the neural tube and the foregut impairs the formation and /or positioning of the tracheal-esophageal septation. A teratogenic insult may occur at a time critical for foregut separation from the notochord, disturbing the areas that ordinarily undergo rapid proliferation. For example, vertebral and cloacal differentiations are directed by notochord inductive signals, which could account for the vertebral and anal anomalies. In our series that 46/127 (36%) cases of EA had other anomalies. In the series by Hasab et al<sup>9</sup> 60% cases of EA had associated anomaly. Spitz et al<sup>11</sup> reported 47%. Saing H et al<sup>12</sup> and Rokitansky et al<sup>2</sup> reported 59% and 52.4% associated congenital malformations.

The reason of low incidence of associated anomalies in our series was that those patients of EA who were born with low birth weight and from remote areas where deliveries are conducted at home did not survived long enough to reach tertiary referral centre. Early gestational age and lower birth weights were significantly correlated with higher rate of malformation. The survival rate in EA with associated congenital anomalies is only 49% as compared to Isolated EA (78%). This shows that association of other congenital anomalies plays a major role in survival of patients of EA in India ( $\chi^2 = 19.497$ ; p<0.001). In our series no patient survived with VACTERL association because of lack of advanced neonatological backup. Saing H et al<sup>12</sup> reported that the association of two or more system anomalies and the severity of associated anomalies influence mortality in esophageal atresia. Survival rate in our series of EA with congenital heart disease is 33% while in series of Ein et al<sup>13</sup> 64% of neonates of esophageal atresia with congenital heart disease survived. Congenital heart disease is the most common malformation associated with EA.<sup>1,14,15</sup> Survival in patients with EA and normal heart is excellent; this reflects advances in surgery and neonatal care of previously high risk groups such as low birth weight infants and infants with cardiac problems.<sup>16</sup> High prevalence of congenital heart disease is an indication for screening. Antenatal Detection of EA should prompt referral for

Associated anomaly	Number of cases	Percentage
Vertebral and Nervous system	8	6.3
Spinal anomalies (hemivertebra, scoliosis, vertebral fusion)	6	4.72
Lumbosacral anomalies	1	0.79
Hydrocephalus	1	0.79
Gastrointestinal system	15	11.81
High ARM	10	7.87
Low ARM	2	1.57
Duodenal atresia	2	1.57
Annular pancreas	1	0.79
Cardiac	17	13.39
Congenital heart disease	17	13.39
Musculoskeletal anomalies	6	4.72
Limb anomalies	4	3.15
Polydactyly	1	0.79
CTEV	2	1.57
Rt. Radial hypoplasia	1	0.79
Rib anomalies (13 <sup>th</sup> rib)	3	2.36
Head and Neck	2	1.57
Cleft lip	1	0.79
Genitourinary system	2	1.57
Hypospadias	2	1.57
Respiratory system	2	1.57
Pulmonary hypoplasia	1	0.79
Tracheomalacia	1	0.79

**Table-1:** Association of other congenital anomalies in patients of esophageal atresia

Multiple anomalies (VACTERL Association)	Number of cases	%
Duodenal atresia + Anorectal malformation	1	0.79
Duodenal atresia + Anorectal malformation + Congenital heart disease	1	0.79
Rib anomalies + Pulmonary hypoplasia	1	0.79
Congenital heart disease + Hypospadias	1	0.79
Congenital heart disease + Meningomyelo-coele	1	0.79
Cardiac disease + Rt. radial hypoplasia	1	0.79

**Table-2:** Associated multiple anomalies with EA



**Figure-1:** Right radial hypoplasia associated with Esophageal Atresia.

detail fetal cardiac scanning. If there is no antenatal diagnosis, timing of post natal screening for cardiac disease (whether it should be performed urgently before surgery) is debatable and there are different recommendations about this.<sup>17,18</sup> Therefore, if the baby is acyanotic with no sign of cardiac disease, we agree with Spitz et al<sup>17</sup> that a preoperative cardiac evaluation is not mandatory and can be deferred until after EA repair. The level of the associated anorectal malformation was not associated with the type of esophageal atresia.

In our study EA with GI anomalies, GI anomalies were responsible for mortality in 4 cases out of 39 (10 %). while in series of Andrassy et al.<sup>19</sup> GI anomalies were responsible for mortality in 5/15 (33 %). In our series the associated urogenital anomalies are less it means there is some environmental or hereditary factor responsible for this. According to van Heurn LW et al<sup>20</sup> the European patients had a significantly higher incidence of urogenital (UG) anomalies as compared to the Asian population (26% vs. 4%), agenesis in 4 and dysplasia in 3 cases of one or both kidneys. Hereditary factors may influence the incidence of associated anomalies in patients of EA particularly of the UG system. Presence of rib,<sup>7</sup> vertebral<sup>6</sup> and limb anomalies do not affect the survival directly but they are usually associated with long gap so associated with morbidity and mortality related with surgical complication (anastomotic leak) as in our study the survival is good in short gap as compared to long gap atresia (91%vs53%). In developed countries the approach for treating EA with associated congenital anomalies is quite different because of advancement in neonatological setup and paying power is not a problem but in developing countries the scenario is different, advanced neonatological backup is limited and most of the patients are from low socioeconomic status, lack of awareness regarding health insurance and treatment facility (expenses in investigation and medication) is not provided by the government.

## CONCLUSION

So we conclude associated anomalies are the leading cause for morbidity and mortality and Waterston prognostic criteria is good for evaluation for prognosis. Presence and severity of other anomalies does not influence the basic approach to treatment of the EA.

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