Purpose: To identify complications, their incidence and risk factors for their occurrence in patients of esophageal atresia (EA) in the 1st year after discharge following surgery.

Materials and Methods: Cases of EA discharged after surgical intervention in the period of July 2011–July 2013 were considered a cohort. All data regarding demographics, investigations, surgical procedure, outcome, and follow-up were recorded.

Results: Seventy-six such patients were discharged in the study period, six of whom were lost to follow-up, and hence, seventy patients were included in the study. Of these 70, 48 (69%) had esophageal continuity restored (46 EA + tracheoesophageal fistula [TEF]; 2 pure EA), while 22 (31%) had been diverted (3 pure EA; 8 EA + TEF following major leak; 11 long gap EA + TEF). Risk of developing any complication (except death) was 48/70 (68%; 95% confidence interval [CI] = 57.4–79.7). Twenty-six of 48 patients with esophageal continuity restored, demonstrated narrowing on contrast study (54%; 95% CI = 39.5–68.7) but only 18 of these 48 (37.5%) had dysphagia. Thirty-one of seventy had an episode of lower respiratory tract infection (LRTI) (44.2%; 95% CI = 32.3%–56.2%). Poor weight gain was observed in 27/70 (37%), and this was significantly common in diverted patients (63% vs. 25%; \( P = 0.009 \)). Twenty-one of total 70 (30%) patients died within the 1st year following discharge.

Conclusions: Sixty-eight percent of cases developed some complication, while 30% succumbed within the 1st year of life following discharge. The common complications were stricture, LRTI, and poor weight gain. All of these were common in diverted patients.

Keywords: Congenital malformation, esophageal anastomosis, esophageal atresia, tracheoesophageal fistula
arising in the first few years are a major determinant of morbidity and mortality further in life. Hence, it is essential to recognize the events occurring in these children during the 1st year of life following discharge.

Similarly, the assessment of preoperative risk factors that determine these events and predict outcome is paramount. An insight into these risk factors will allow easy recognition of newborns who may benefit from a more intensive follow-up program. We aim to study the outcome of children with EA ± TEF in the 1st year after discharge, following surgery.

Materials and Methods

Study design and population

It is a retrospective cohort study with a duration of 3 years, i.e., from July 2011 to July 2014. Newborns with EA ± TEF successfully discharged after surgical intervention at our institute were included in the study. Those operated elsewhere and referred to our center for specialized care, were excluded. Infants who did not report for follow-up (despite repeated telephones and letters) after discharge were considered lost to follow-up and were also excluded from the study.

Management protocol

Newborns with EA-TEF had undergone preoperative investigations including chest X-ray (with red rubber catheter in situ); echocardiography (ECHO) to rule out lethal cardiac anomalies and an ultrasound examination of the abdomen to rule out renal anomalies requiring immediate attention. After stabilization, an extrapleural right posterolateral thoracotomy with the division of fistula and primary anastomosis is possible in the majority of cases. Postoperatively, these neonates had been managed in our neonatal surgical intensive care unit. All of them had been subjected to elective mechanical ventilation for 48–72 h. Other measures, including frequent guarded pharyngeal and oral cavity suctioning, antibiotics, analgesics, and nutrition (Nasogastric (NG) feeds or parenteral nutrition), were also ensured. Children from esophageal continuity group were anticipated to have GER at the time of discharge and were started on anti-GER measures. Contrast study (oral contrast swallow) is usually performed after 1 week (day 7–10 postoperatively) to identify anastomotic leaks. Patients in whom esophageal anastomosis could not be performed or had major leak were diverted. In these patients, the proximal esophagus was brought out as an esophageal stoma for egress of saliva and gastrostomy or abdominal esophagostomy was created for feeding.

Data collection

Data were collected from admission records, case files, operative notes, discharge summaries, and follow-up files. Detailed information about birth-related events, demographic profile, type of EA, associated anomalies and risk factors, operative procedure, postoperative events, and complications were extracted.

Definitions

Cardiac anomaly

Any cardiac anomaly detected on preoperative ECHO was considered as the presence of a cardiac anomaly. It was considered as major if it required medical or surgical intervention.

 Anastomotic leak

Any leakage of contrast seen in the postoperative contrast study was considered as anastomotic leak, irrespective of symptoms. Leaking of the majority of the contrast with little passage of contrast in the distal esophagus was considered a major leak.

 Stricture

Any narrowing seen on contrast study performed after discharge along with the presence of dysphagia or if the child underwent any dilatation after discharge.

 Condition of esophagus at discharge

All patients with intact esophageal repair and accepting oral feeds at discharge were included in “esophageal continuity” group. Others who had cervical esophagostomy for drainage of saliva and gastrostomy or thoracic esophagostomy or abdominal esophagostomy for feeding were included in the “diverted esophagus” group.

 Lower respiratory tract infection

It was defined as either the presence of fever with cough and crepitation heard on auscultation or fever with chest X-ray showing consolidation.

 Gastroesophageal reflux

All patients in the esophageal continuity group were anticipated to have GER at the time of discharge and were started on anti-GER measures. Those with regurgitation of feeds despite conservative measures were subjected to a contrast study or GER scan to document severity of GER.

 Death

Any patient dying within 1 year from the date of discharge was considered as a death in the study group. For children dying in the hospital, the cause of death was recorded. Death occurring at home was confirmed telephonically, and the possible cause was noted.

 Follow up visits

The total number of follow-up visits during the 1st year after discharge was noted. A visit was considered routine
if the patient came for routine follow-up irrespective of the symptoms. Any visit in which child was sick enough to warrant urgent evaluation and admission in the hospital was considered an emergency visit.

**Statistical analysis**
Data entry was done using Microsoft Excel. Data analysis was done using IBM SPSS Statistics 25 (IBM, New York, USA). Risk of developing various complications was derived from the entire cohort. The risk estimates were compared between preoperative factors, and \( P \) value was calculated. Univariate analysis was done for comparison between groups. The relative risk (RR) of developing a complication between the two groups was found. Kaplan–Meier survival estimates were calculated for the entire cohort and survival estimates between various groups were compared for any significant difference.

**Consent and approval**
Parental consent was obtained before enrollment into the study. A patient information sheet was explained to the parents and consent form for participation duly signed. Parents not giving consent were not included. Ethical clearance was obtained from the Institutional Review Board before starting the study.

**Results**

**Description of the cohort**
During the study period, 106 neonates with a diagnosis of EA ± TEF had been admitted under our care. Of these, 101 were operated upon and 76 were discharged in satisfactory condition from the hospital. We were unable to contact six infants, and they were considered loss to follow-up. Therefore, only seventy children completed 1 year of follow-up and were enrolled in this study. There was a slight male preponderance (43/70; 61%) in our study. The proportion of premature infants was approximately 36% (25/70). The detailed distribution of the cohort and the inpatient course is depicted in Figure 1.

**Figure 1:** Distribution of cohort \((n = 70)\); EA + TEF: Esophageal atresia with tracheoesophageal fistula, EA: Esophageal atresia, TEF: Tracheoesophageal fistula

**Associated anomalies**
Of the total 70 newborns, 59 (84%) had other associated anomalies. While 38/70 (54.3%) had only one associated anomaly, 13/70 (18.6%) had two, and 8/70 (11.4%) had more than two associated anomalies. Table 1 depicts the frequency of congenital anomalies associated with EA.

**Condition of esophagus at discharge**
At the time of discharge, there were 48 (69%) children with esophageal continuity group and 22 (31%) in diverted esophagus group.

**Anastomotic leak**
Leak rate in our cohort [Figure 1] was 25% (14/56) and nearly 65% (9/14) of these had a major leak. Five patients had a minor leak which had been managed conservatively.

**Complications following discharge**
Of the total 70 infants, 48 (68%) had some complication during the first 12 months following discharge.
in diverted esophagus group had 1.23 times higher risk for developing any complication in the 1st year, but the difference was not statistically significant ($P = 0.2$) [Table 2].

### Anastomotic stricture

Seventeen of the total 48 newborns (35%) in esophageal continuity group had stricture postoperatively. Six of the 48 patients in esophageal continuity group had a history of leak and 5 of these 6 (83%) developed stricture later. Of the 42 patients without any history of leak, 12 (29%) developed stricture. The risk of developing a stricture in those with a history of leak is almost 2.9 times greater than in those without leak (83% vs. 29%; RR 2.86; 95% confidence interval [CI] 1.61–5.30). The difference is statistically significant ($P = 0.0004$).

### Lower respiratory tract infections

Thirty-one (44.2%) children developed lower respiratory tract infection (LRTI) during follow-up. The incidence of LRTI in the diverted group (11/22; 50%) and esophageal continuity restored group (20/48; 41.6%) was comparable ($P = 0.5$). In addition, the difference in the incidence of LRTI between patients with (26/51; 50.9%) and without cardiac anomaly (5/28; 27.7%) did not reach statistical significance ($P = 0.08$).

### Gastroesophageal reflux

GER was anticipated to be present in all cases and at discharge anti-GER measures were instituted in all.

A total often patients underwent GER scan to document GER, and it was positive in nine cases.

### Poor weight gain

Poor weight gain was seen in 26 (37%) children. Out of these, 14 (64%) belonged to the diverted esophagus group, while 12 (25%) children were from esophageal continuity group. This difference in the incidence of poor weight gain between these two groups was statistically significant ($P = 0.0017$).

### Stoma complications

Only two newborns developed stoma-related complications during follow-up. One of them developed recurrent bleed from the abdominal esphagostomy site which had been managed conservatively. The other newborn developed stenosis of the cervical esphagostomy site for which revision had to be done twice.

### Survival outcome in the 1st year following discharge

In this cohort, 21 (out of 70) children died during the 1st year, thus giving the 1-year overall survival (OS) of 70% (95% CI 58%–79%). The survival at 3 months was 81.4% (95% CI 70.1%–88.7%). The survival at 6 months was 74.2% (95% CI 62.3%–79.2%).

### Survival outcome according to the esophageal continuity

The 1-year OS was significantly low [Table 3 and Figure 2] in children with diverted esophagus as compared to those with maintained continuity (45.4% vs. 81.25%, respectively) ($P = 0.017$).

### Survival outcome according to maturity at presentation

During the 1-year follow-up, a total of 12 deaths occurred in the preterm group and 9 in term group. In the preterm newborns, the majority of deaths

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**Table 1: Associated congenital anomalies in the cohort**

| Congenital anomalies     | n (%) |
|--------------------------|-------|
| Cardiovascular           | 51 (72) |
| Vertebral                | 5 (7) |
| VACTERL                  | 2 (2.8) |
| Anorectal malformation   | 4 (5.7) |
| Gastrointestinal         | 3 (4.2) 1 each with duodenal atresia, pyloric stenosis, and annular pancreas |

**Table 2: Risk of developing complications in the first 12 months following discharge**

| Group                           | Number of patients | Frequency (%) | Risk of any complication | Relative risk |
|---------------------------------|--------------------|---------------|--------------------------|---------------|
| **Type of atresia**             |                    |               |                          |               |
| EA + TEF                        | 65                 | 45 (69.2)     | 0.6                      | 1.15          |
| EA                              | 5                  | 3 (60)        |                          |               |
| **Status of esophagus at discharge** |                |               |                          |               |
| Maintained continuity           | 48                 | 35 (72.9)     | 0.2                      | 1.23          |
| Diverted                        | 22                 | 13 (59.1)     |                          |               |
| **History of anastomotic leak** |                    |               |                          |               |
| Yes                             | 14                 | 10 (71.4)     | 0.8                      | 1.03          |
| No                              | 42                 | 29 (69)       |                          |               |
| **Cardiac anomaly**             |                    |               |                          |               |
| Present                         | 51                 | 37 (72.5)     | 0.1                      | 1.3           |
| Absent                          | 19                 | 10 (55.5)     |                          |               |

EA: Esophageal atresia, TEF: Tracheoesophageal fistula
First-year follow-up of neonates with EA

Dey, et al.: First-year follow-up of neonates with EA

In our study, cardiovascular anomalies were most common (72%). Of these, 15 were major and 36 were minor. This was followed by vertebral (7%) and VACTERL anomalies (2.8%), etc. As compared to the study by Seo et al.,[6] a higher incidence of associated cardiac anomalies was noticed in our study (72% vs. 35%). However, the incidence of major cardiac anomalies was the same in our cohort and in the literature (21.4% and 21%, respectively).[6]

Table 3: Overall survival within different subgroups

| Group, n | Number of deaths | 1-year OS, % | P  | Relative risk of death |
|----------|------------------|-------------|----|------------------------|
| Type of atresia | | | | |
| EA ± TEF, 65 | 19 | 70.7 | 0.5 | 1.86 |
| EA, 5 | 2 | 60 | | |
| Status of esophagus | | | | |
| Diverted, 22 | 12 | 45.4 | 0.001 | 3.71 |
| Maintained continuity, 48 | 9 | 81.25 | | |
| Maturity at presentation | | | | |
| Preterm, 25 | 12 | 52 | 0.015 | 3.09 |
| Term, 45 | 9 | 80 | | |
| Development of LRTI | | | | |
| Yes, 31 | 13 | 58 | 0.06 | 2.26 |
| No, 39 | 8 | 79.4 | | |

LRTI: Lower respiratory tract infection, OS: Overall survival, EA: Esophageal atresia, TEF: Tracheoesophageal fistula

Survival outcome according to development of lower respiratory tract infection

The difference in 1-year OS among the two subgroups – one with LRTI and the other without any LRTI episodes during follow-up was high but did not reach statistical significance (P = 0.06).

DISCUSSION

EA ± TEF are common congenital anomalies.[4] Over the years, there has been a significant reduction in the mortality of newborns born with EA. This is due to early diagnosis, advanced neonatal intensive care, and improved surgical techniques. It has also led to an increase in the incidence of associated anomalies in children who are treated for EA.[5] In our study, cardiovascular anomalies were most common (72%). Of these, 15 were major and 36 were minor. This was followed by vertebral (7%) and VACTERL anomalies (2.8%), etc. As compared to the study by Seo et al.,[6] a higher incidence of associated cardiac anomalies was noticed in our study (72% vs. 35%). However, the incidence of major cardiac anomalies was the same in our cohort and in the literature (21.4% and 21%, respectively).[6]

The anastomotic leak may result from ischemia of the esophageal ends, excess anastomotic tension, sepsis, poor suturing techniques, extensive mobilization of the distal pouch, and increased gap length. The reported incidence of an anastomotic leak following repair of EA ranges from 14% to 21%, and only one-third of these are major leaks.[7] When compared with the literature, the incidence of anastomotic leak and the proportion of major leaks were more in our cohort.[8‑11] Esophageal strictures have been reported to occur in 6%‑40% of cases of EA.[12] This variation in the incidence of stricture is due to different operational definitions of stricture in the studies. The risk factors implicated in stricture formation include anastomotic tension, anastomotic leak, and GER. In our study, 35% of neonates with restored continuity of esophagus had a stricture at the anastomotic site. Dysphagia was present in more than two-thirds of these children. We also observed a significantly higher risk of developing stricture in children with a history of anastomotic leak.

Respiratory complications are major causes of late death in children with EA-TEF. These can be due to GER, aspiration, reactive airway, and tracheomalacia, etc.[13] During follow-up, 60%‑80% of the children with EA-TEF tend to develop LRTI.[14] Abnormal pulmonary function tests have been reported in up to 96% of children, adolescents, and adults who are previously treated for EA-TEF.[15] Incidence of pneumonia in our cohort was more than 40%. No significant difference was seen in children with diverted esophagus as compared to those with restored continuity.

GER, due to esophageal shortening and loss of lower esophageal sphincter, is a common complication after surgical correction of EA ± TEF. It has been suggested...
that around 40% of infants have GER necessitating treatment during follow-up. Half of these children are managed successfully with medical therapy to suppress gastric acid production, and the remainder may require a fundoplication. 

During follow-up, GER was managed conservatively in all cases. None of them required an antireflux surgery.

Poor weight gain and failure to thrive is another common complication in infants operated for EA. According to literature, 48% of these infants weigh below the tenth centile for their age at 1 year. Poor weight gain was seen in more than one-third (37%) of our study population. The complication was significantly more in children with a diverted esophagus as compared to those with restored continuity. This is unexpected, as the children with diverted esophagus are more likely to gain weight on gastrostomy or abdominal esophagostomy feeds as compared to the esophageal continuity group, in whom stricture and dysmotility often cause feeding difficulties. The above can be explained by many factors. First and foremost, children in the esophageal continuity group are relatively easy to feed. Frequent breastfeeding by the mother is sufficient to meet their daily nutrition requirement. However, feeding children with the diverted esophagus is a tedious task. Breast milk needs to be expressed, stored, and warmed before every feed. If formula milk is used, it also needs a similar preparation. The feed had to be then administered meticulously through the tube. This can lead to a decrease in the frequency of feeding and poor nutrition in the diverted esophagus group. Second, frequent dislodgements of the gastrostomy tube can also affect the feeding and weight gain of the child. Third, inadequate nursing of the child at home leads to maceration near the stoma site and secondary infections which ultimately affect the nutrition of the child. Furthermore, continuous drainage of saliva from the neck of the child requires constant supervision and care. In developing countries, this can add to the monetary burden on the parents leading to child neglect.

We noticed a maximum number of deaths (13/21, 62%) during the first 3 months of life. This is because, in developing countries, the majority of parents do not return back to the tertiary care hospital for follow-up visits due to monetary issues. Further, most of the follow-up visits occur at peripheral and ill-equipped hospitals. This fact highlights the need for closer follow-up of these patients immediately after discharge for at least the first 3 months. Most parents also complain that no treatment is administered to the child in local hospitals, and the child is referred to our center even for fever. This delays the elementary treatment and increases morbidity and mortality. Better coordination with the local health providers can address this situation. Educating and training parents in basic maneuvers such as oral suctioning to in children with swallowing difficulty, proper positioning of child and burping to prevent reflux and aspiration, and care of gastrostomy tubes are crucial measures to prevent complications. We observed a comparatively low 1-year OS in children with the diverted esophagus [Table 3]. In our study, poor weight gain and failure to thrive are the single most important factor contributing to higher mortality observed in the diverted esophagus group. Second, those diverted following leak have a much more chance of pulmonary morbidity due to complications such as pneumonia, mediastinitis, and empyema. Third, complications associated with stoma including poor hygiene causing secondary infections, feeding affected by frequent dislodgements of gastrostomy tube may also contribute to mortality. Last but not the least, it has highlighted in the literature that children with pure EA and long gap EA ± TEF (both of which form the majority of diverted esophagus group) have a higher incidence of associated congenital anomalies and can contribute to a poor overall outcome.

A relatively higher risk of death (2.26 times) was observed during the follow-up period in those developing LRTI when compared to those without LRTI [Table 3]. This can be explained by the fact that pneumonia by itself is a major cause of mortality. During the 1st year of follow-up, deaths were significantly higher in preterm infants as compared to term babies [Table 3]. Most preterm newborns died within the first 3 months of life. Thus, these preterm infants must be enrolled in an intensive follow-up program during the 1st year of life to ensure better survival.

Conclusions

Thirty percent of children with EA ± TEF, who were operated and discharged, die within the 1st year of life. Two-thirds of these deaths occurred within 3 months of age. The risk of developing any complication (except death) following discharge is 68%. This risk is more in children with diverted esophagus as compared to those with esophageal continuity. One-year OS is significantly low in diverted esophagus group and preterm newborns.

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Conflicts of interest
There are no conflicts of interest.
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