Impact of the various factors on survival of tracheoesophageal fistula patients: A prospective study of 16 patients

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Abstract
Introduction: Tracheoesophageal fistula (TEF) is one of the common congenital anomalies presented at birth. Management of TEF is a challenging task as outcome of these cases not only depends on surgeon and anaesthesiologist’s skills but also depends on various factors associated with new born. This prospective study evaluates the association of various factors on survival of TEF patients.

Materials and Methods: 16 newborn patients in a calendar year were enrolled in this prospective study and impact of various factors like age, weight, parity of mother, associated congenital anomalies and family history, mode of delivery, place of delivery, associated hydramnios and type of TEF were evaluated on the survival of neonates born with TEF.

Results: Male, female ratio was equal. Patient with birth weight >2.5 kg had higher survival rate (100%) compared to patient <2.5kg weight (23.08%). No other factors significantly influence the survival rate of neonates with TEF.

Conclusion: Birth weight remains the single most important predictor of mortality among TEF patients, as suggested with Waterston risk classification.

Keywords: Tracheoesophageal fistula, Birth weight, Neonates, Waterston classification.

Introduction
‘Esophageal atresia & tracheoesophageal fistula (TEF)’ is one of five major surgical manifestations of first week of life including congenital diaphragmatic hernia (CDH), omphalocele, gastrochisis, intestinal obstruction and meningomyelocele. In these CDH, omphalocele and meningomyelocele are presented at birth while TEF and intestinal obstruction take hours or days to manifest.

Incidence of TEF is 1:3000 live birth, approximately 87% consist of a fistula from distal trachea to the esophagus and a blind proximal esophageal pouch.¹ It occurs due to embryological defect results from imperfect division of the foregut into the anteriorly positioned larynx, trachea and posteriorly positioned esophagus which occurs at the fourth and fifth week of intrauterine life.

These cases are usually present with aspiration pneumonitis and respiratory distress due to aspiration of gastric content, secretions and breastfed milk from a blind upper esophageal pouch into trachea. Dehydration results from the fact that the proximal esophagus doesn’t communicate with stomach. It demands early diagnosis, resuscitation, treatment and emergency surgical correction.

Association of congenital anomalies worsens the outcome (as described by Waterston's classification and later by spitz in 1990).²

Along with early diagnosis and management, anaesthetic management is also challenging because these neonates usually present with low birth weight, associated congenital anomalies, respiratory tract infection, risk of hypothermia and dehydration. Even after good anaesthetic management and surgical correction neonates need skilled nursing staff, besides all modern neonatal intensive care facilities.

We planned this study to evaluate the association of different factors on survival of TEF patients.

Materials and Methods
After institutional ethical committee approval, this prospective study was carried out in MB Govt. Hospital, RNT Medical College, Udaipur which included the neonates scheduled for repair of esophageal atresia and tracheoesophageal fistula in routine and emergency operation theatres.

All the patients were enquired about obstetric history (parity, previous born child, week of gestation, presence of hydramnios, mode of delivery: (vaginal/assisted/caesarean, delay in birth), clinician notes (including APGAR score, weight at birth, need for resuscitation), mother’s medical/drug history, family history of having any congenital anomalies, time of diagnosis after birth and by whom, any feed/fluid given in between birth and diagnosis, presenting complaints, delivery at institute or at periphery and measures taken before presenting to hospital and treatment given after admission were noted.

After getting informed consent, baby was examined thoroughly including complete physical examination, routine laboratory investigation (CBC, BT, CT, X-ray chest) including neonatologist examination record and other relevant investigations

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according to manifestations of other congenital anomalies.

Patients with preoperative pneumonitis were optimized with medical intervention (e.g., oxygenation, humidification, physiotherapy, bronchodilators, cortisone, antibiotics, i.v. fluids and temperature regulation, etc.) before taking for surgery. Consent from patient's parents/attendants was taken and crossmatched blood was made available in operation theatre.

Intraoperative fluid therapy included deficit correction, maintenance fluid (4 ml/kg/hr of 5% dextrose with N/4 normal saline) and blood if needed. Baby was wrapped in cotton layer to prevent hypothermia.

After securing a peripheral line with 24 gauze intravenous canula, baby was premedicated with inj. Glycopyrrolate (0.005-0.01 mg/kg) and Inj. Fentanyl (2mcg/kg). Patients were induced with Inj. Thiopentone (5-7mg/kg) and Inj. Succinylcholine (1-1.5mg/kg).

Intubation was accomplished with appropriate sized non cuffed portex PVC endotracheal tube and anesthesia was maintained with O₂ (50%) + N₂O (50%) + Sevoflurane and muscle relaxant Inj. Atracurium 0.5 mg/kg I.V as bolus initially then 0.5mg/kg/hr infusion.

At the end of surgery intercostal nerve block/local infiltration of incision line was done by surgeon with inj. Bupivacaine (2 mg/kg diluted in normal saline to make concentration 0.25%) for postoperative pain relief. Residual muscle paralysis was reversed with inj. Neostigmine (0.06-0.08 mg/kg) plus inj.glycopyrrolate (0.005-0.01 mg/kg) and extubation was done after achieving normal muscle activity (limb movement), regular normal respiratory pattern, spontaneous eye opening; otherwise baby was kept intubated and shifted to neonatal ICU for ventilatory management Postoperative recovery, morbidity, duration of hospital stay was noted.

**Observations**

In present study 18 patients were enrolled (over a study period of 1 year) but 2 patients left against medical advice before any intervention; finally 16 patients were studied and following observations were noted: 9 patients were admitted in 24 hours of birth while 7 patients were admitted after 1 day of birth in our institute. Patients with age > 1 day at admission had higher survival rate (42.86%) compared to patients with age ≤ 1 day (33.33%) which was found statistically non significant (p=0.367).

In our study 3 patients had weight ≥ 2.5 Kg and 13 patients had ≤2.5 Kg. Patients with weight ≥ 2.5 kg at admission had statistically higher survival rate (100%) as compared to patients with weight < 2.5 kg (23.08%). (Table 1)

In our study male and female were equal (8 each) and there was no significant association found between sex of patient and survival rate.

There were 14 patients of >37 weeks and 2 patients were < 37 weeks gestational age and survival rate was higher in patients > 37 weeks (42.86%) compared to <37 weeks (0%) which was statistically insignificant. (p=0.375)

Total 11 patients (68.75%) were associated with polyhydramnios, out of which 5 patients (45.45%) were survived while 5 patients had no association with polyhydramnios in which only 1 patient survived. (statistically insignificant p= 0.288).

15 patients delivered spontaneously in which 5 patients (33.33%) survived, while 1 delivered with caesarian section and survived. Thus Mode of delivery shows no statistically significant association (P = 0.375) with survival.

4 patients were born from primigravida in which only 1 patient (25%) survived. 12 patients were born from multigravida in which 5 patients (41.67%) survived. Patients born to multigravida mother had higher survival (41.67%) as compared to patients born to primigravida mother (25.00%). Parity of mother had no statistically significant association with survival (P = 0.396).

15 patients had no history of congenital anomalies in family out of which 6 patients survived while only 1 patient had positive family history that was not survived. Thus family history of congenital anomaly had no statistically significant association with survival (P = 0.625).

The survival rate was 27.27% in patients present with drooling / frothing; 28.57% in patients with pneumonitis and none in patients with associated congenital anomaly. These clinical findings had no statistically significant association with survival. (Table 2)

In our study 15 patients had type III b of TEF while 1 patient had III a TEF and found no significant correlation with survival.

Patients were grouped as per Waterston’s classification and survival was 100% in Group A, 44.44% in Group B and 0% in Group C (statistically significant P = 0.037). (Table 3)

15 patients were extubated immediately after surgery while 1 patient was shifted intubated in ICU. Delayed extubation showed no statistically significant correlation with survival (p=0.194)

In our study most common postoperative complication was pulmonary (68.75%).

The mean duration of hospital stay was more (10.17 days) in patients who survived compared to that did not survive (5.10 days). (p=0.02)
were similar. Our results were consistent with those of Yang et al (59.38%). In our study, 81.25% patients weighed < 2.5 kg while 18.75% patients had weighed ≥ 2.5 kg. Overall survival rate was 66.5% which was comparable with Yang et al (53.33%), Verma et al (60%) while survival in > 2.5 kg wt patient was similar to Fliston et al and Calverley et al.

In our study no statically significant association was found between gestational age and survival rate. Since the number of patients with gestational age < 37 weeks is very small in both our study and Yang et al (2 and 3, respectively); no statistically significant conclusion could be drawn whereas, survival in patients with gestational age ≥ 37 weeks is found to be comparable with other studies. Our results were comparable to Yang et al (80%) and Fliston et al. In our study 93.75% babies were delivered at our hospital while 9 patients were admitted from other hospitals. During this period 16677 deliveries were conducted in our institute which denotes that incidence of babies with TEF was 1:2382 which was comparable to observations made by Yang et al (1:2400-4500) and other studies like Barash et al (1:3000).

In our study patients having age at admission ≤ 1 day were 56.25% and with age > 1 day were 43.75%. Survival with age ≤ 1 day was 33.33% while it was 42.86% in >1 day age. Calverley et al attempted to identify the impact of age at admission in two prospective studies in 1963 and 1968. Age at admission ≤ 1 day was 32.69% and 36.14% respectively in the two studies while it was 67.31% and 63.60% > 1 day. There was no effect of the age at admission on the outcome in either of these studies. Present study also fails to demonstrate any effect of age at admission on the outcome.

In present study male, female ratio was equal (50% each) and there was no statistically significant difference regarding survival in both sexes, similarly Yang et al also found no impact of sex of patients on their survival.

Table 1: Weight of patients

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Survival</th>
<th>Non-survival</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>≥ 2.5</td>
<td>3</td>
<td>100.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; 2.5</td>
<td>3</td>
<td>23.08</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>100.00</td>
<td>10</td>
</tr>
</tbody>
</table>

P = 0.036

Table 2: Clinical presentation (signs and symptoms)

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Survival</th>
<th>Non-survival</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Drooling / frothing</td>
<td>3</td>
<td>27.27</td>
<td>8</td>
</tr>
<tr>
<td>Inability to feed</td>
<td>3</td>
<td>28.57</td>
<td>5</td>
</tr>
<tr>
<td>Crepts/ pneumonitis</td>
<td>3</td>
<td>27.27</td>
<td>8</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>0</td>
<td>0.00</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3: Waterston’s pre-operative risk classification

<table>
<thead>
<tr>
<th>Group</th>
<th>Criteria</th>
<th>Survival</th>
<th>Non-survival</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Wt. &gt; 2.5 kg and well</td>
<td>2</td>
<td>100.00</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>Wt. 1.8-2.5 kg OR wt. &gt; 2.5 kg assoc. with cong. anomaly/ mod. pneumonitis</td>
<td>4</td>
<td>44.44</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>Wt. &lt; 1.8 kg OR Wt. 1.8-2.5 kg assoc. with severe pneumonitis/ cyanosis cong. Anomaly</td>
<td>0</td>
<td>0.00</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>100.00</td>
<td>10</td>
<td>100.00</td>
</tr>
</tbody>
</table>

P = 0.037

Discussion

TEF is considered a touchstone in pediatric surgery and these cases are usually complicated due to delayed presentation with aspiration of gastric juice or from spillage of secretions or breastfed milk from a blind upper pouch leading to pneumonia, respiratory distress and dehydration. It demands early diagnosis, resuscitation, treatment and emergency surgical correction. Association of congenital anomalies further worsens the outcome.

In our study 7 patients were delivered at our hospital while 9 patients were admitted from other hospitals. During this period 16677 deliveries were conducted in our institute which denotes that incidence of babies with TEF was 1:2382 which was comparable to observations made by Yang et al (1:2400-4500) and other studies like Barash et al (1:3000).

In our study patients having age at admission ≤ 1 day were 56.25% and with age > 1 day were 43.75%. Survival with age ≤ 1 day was 33.33% while it was 42.86% in >1 day age. Calverley et al attempted to identify the impact of age at admission in two prospective studies in 1963 and 1968. Age at admission ≤ 1 day was 32.69% and 36.14% respectively in the two studies while it was 67.31% and 63.60% > 1 day. There was no effect of the age at admission on the outcome in either of these studies. Present study also fails to demonstrate any effect of age at admission on the outcome.

In our study, 93.75% babies were delivered by spontaneous vaginal birth, while 6.25% were delivered by LSCS. Survival rate among spontaneous vaginal...
delivery was 33.33% and in group of LSCS was 100% (only single case). Verma et al.\(^3\) showed that mode of delivery was spontaneous vaginal in 84% patients and 16% patients were delivered by LSCS. This difference might be due to obstetrician choice, availability of surgeon and protocols that vary among different institutes.

In our study 25% of mothers to whom patients of TEF born were primigravida and 75% mothers were multigravida. Survival rate of neonates, born to primigravida mother was 25% while it was 41.67% in multigravida mother. There was no other literature to compare the data.

In our study 6.25% neonates (one case) had family history of congenital anomaly and this neonate was expired. There was no data available to compare with this observation.

In present study, 68.75% patients were admitted with drooling of saliva and pneumonitis. Verma et al.\(^5\) found that 88% patients had Pneumonitis preoperatively. Ahmed et al.\(^7\), Fliston et al.\(^6\), Calverley et al.\(^4\) found its incidence 52%, 43.75% and 48.2% respectively.

In our study there was no statistically significant correlation between survival and type of TEF. Yang et al.\(^3\), Ahmed et al.\(^5\) and Calverley et al.\(^4\) also supports our results.

In our study according to Waterston’s criteria, patients belonging to Group A were 12.5%, Group B 56.25% and Group C were 31.25%. Survival rate for Group A, Group B & Group C patients were 100%, 44.44% and 0% respectively. These results were comparable to other studies mentioned in Table 4.

In our study survival for Group A and Group B were found to be comparable to other studies while survival was less in Group C because patients had reported with severe respiratory distress and cyanosis, while in Calverley et al.\(^4\) study the survival rate in Group A was improved as they have done staged repair which reduces gastric reflex and time to control infections aiding in improvement of neonatal condition.

In our study, 93.57% of patients were immediately extubated and 6.25% patients shifted to neonatal ICU intubated. Survival in patients with immediate extubation was 33.33% and 100% in patient with delayed extubation (only one patient). The study conducted by Ahmed et al.\(^7\), 95.65% patients were shifted intubated to ventilator while 14.46% patients were shifted to ventilator and survival rate was 50% in study conducted by Calverely et al.\(^4\) These results concluded that baby having elective ventilatory therapy showed better outcome. In our setup at study time we are not having neonatal ventilatory facility so early extubation and oxygen by hood was in practice.

In our study most common postoperative complications were pulmonary (68.75%) which were comparable with Yang et al.\(^3\) (50%) and Calverely et al.\(^4\) (69.23%).

In our study mean hospital stay was 10.17±3.06 days in survivors as compared to 5.10±2.28 days in non-survivors. Verma et al.\(^3\) reported that mean hospital stay was 18.08±3 days in survivors. No other data were available to compare this observation.

### Table 4: Survival rate in different group in different studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>Incidence</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verma et al. (2002)</td>
<td>Group A</td>
<td>12%</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>56%</td>
<td>57%</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>32%</td>
<td>25%</td>
</tr>
<tr>
<td>Yang et al. (2003)</td>
<td>Group A</td>
<td>17.4%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>47.8%</td>
<td>83.3%</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>34.8%</td>
<td>0%</td>
</tr>
<tr>
<td>Calverley et al. (1968)</td>
<td>Group A</td>
<td>18.07%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>38.55%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>43.38%</td>
<td>59.2%</td>
</tr>
<tr>
<td>In our study</td>
<td>Group A</td>
<td>12.5%</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>56.25%</td>
<td>44.44%</td>
</tr>
<tr>
<td></td>
<td>Group C</td>
<td>31.25%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### Conclusion

In present study we conclude that birth weight remains the single most important predictor of mortality among TEF patients as suggested with Waterston’s risk classification. Age at admission, sex, gestational age at which baby born, mode of delivery, parity of mother, associated congenital anomalies in family and type of TEF don’t have impact on survival of these patients. We suggest that better neonatal ICU facility, trained staff and optimization of neonate before surgery can be a milestone to improve outcome in TEF patients.

### Conflicts of Interest: None.

### References
