

# Management of associated anomalies of oesophageal atresia and tracheo-oesophageal fistula

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## ABSTRACT

Tracheo-oesophageal fistula (TEF)/oesophageal atresia is one of the most common and serious congenital malformation. Despite progresses made in the field of early diagnosis, surgical techniques, ventilatory support and control of chest infections; morbidity and mortality still remains quite high and differs a lot from one to another centre particularly in the developing countries; as the availability and the level of neonatal care facilities are different. Associated anomalies play a significant role in dictating the outcome, timing of intervention and even the approach to management. The objectives of this review article is to outline the spectrum of associated anomalies, emphasise need of standardised system of documentation of anomalies, prognosis and management issues that would influence timing and approach of TEF repair.

**Key words:** Associated anomalies, oesophageal atresia, trachea-oesophageal fistula

## INTRODUCTION

The incidence of various associated anomalies with trachea-oesophageal fistula/oesophageal atresia (TEF/OA) varies between 40% and 55%.<sup>[1-3]</sup> Anomalies may be single or multiple, minor or major, detected at birth or later on. The life-threatening anomalies require only counselling and no treatment. Major associated malformations need to be detected and treated in time. The minor ones, with no risk to life, require no immediate intervention. The high incidence of association is due

to the early disturbance in organogenesis, which results in OA and other associated anomalies. These anomalies are most common in patients with isolated OA (55-60%) and the least common in cases with H type TEF (25-30%).<sup>[1-5]</sup> Furthermore, the infants weighing <2000 g have almost three times higher incidence of associated anomalies when compared to those weighing more than 2500 g.<sup>[2]</sup>

Infants with OA and other associated congenital anomalies can be divided into following two groups:

**Group A:** Infants with severe anomalies generally incompatible with survival and constitute about 5% cases presenting with isolated OA. For example, trisomy 15, Potter's syndrome, complex-cardiac anomalies, tracheal agenesis and cerebral hypoplasia. These infants preclude further management

**Group B:** Infants with OA having major or minor congenital anomalies but salvageable. More than 95% cases fall into this group.

Those likely to complicate the early life of newborns with OA-TEF. Most of them require some form of surgical intervention early in the child's life.

Babies may be affected by a recognised syndrome (e.g., trisomy) or more than one associated anomalies.

## MINOR ANOMALIES

Not likely to be of significant consequence. May or may not need any surgery and if so, it is probably minimal and can be done at a later date.

## Problems created by classification and documentation systems not universally employed

Due to considerable difference in the methods used and the interest taken, the incidence of specific types of anomalies varies significantly among different

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series [Table 1]. Furthermore, the lack of uniformity in the method of investigation and potential associated anomalies (non-uniform application of renal ultrasound with or without micturating cystourethrography and echocardiography) has resulted in incomparable impacts of these anomalies on the prognosis of these infants.

## RECOMMENDATIONS

Myers *et al.*<sup>[6]</sup> analysed the discrepancies in documentation and classification systems of several large series and formulated some recommendations, which adequately takes care of epidemiological, clinical and therapeutic requirements.

1. Data should be collected prospectively.
2. Routing investigation should include renal ultrasound and echocardiography (as a minimum requirement).
3. The number of associated anomalies should be reported as percentage of the total cohort of patients, rather than as a percentage of the anomalies themselves.
4. True congenital anomalies should be recorded separately from acquired conditions, for example, intracranial haemorrhage, respiratory distress syndrome, hyaline membrane disease etc.
5. Non-life threatening trivial lesions, for example, accessory auricles. Undescended testis, inguinal hernia, umbilical hernia or pre-auricular sinuses should always be specified in the miscellaneous group as consistent reporting of these apparently irrelevant congenital anomalies may ultimately help shed light on the aetiology of OA-TEF itself. In addition, it reduces the likelihood that their inclusion in major categories will distort the overall impact on prognosis.
6. Wide variation in the pact of associated abnormalities on the management and long-term outlook in OA should be recognised.

A method of grading of significance of abnormalities shown in Table 2.

## IMPACT AND MANAGEMENT OF ASSOCIATED CONGENITAL ANOMALIES

Major congenital anomalies are responsible for 55% mortality in OA-TEF patients.<sup>[2]</sup> Of these, 6-11% have trisomy and/or complex cardiac defects which are incompatible with life thereby precluding any active management.<sup>[7]</sup>

Complex cardiac anomalies account for most of deaths (35%). Survival rate falls proportionately with the addition of more defects, for example, 76% survival rate with one additional anomaly and 59% with more than one.<sup>[7]</sup> Various series<sup>[1,2,7]</sup> document one or more than one additional congenital anomaly in 50-70% patients with OA-TEF. VACTERL association has high incidence of major cardiac anomalies (78%) and a high mortality rate (24%).<sup>[8-10]</sup> Kutianawala *et al.*<sup>[9]</sup> also reported more than 70% mortality in their series of 10 cases of TEF cases with the CHARGE association mostly due to severe cardiac anomalies.

System wise associated anomalies are depicted in Tables 3-6.

### Cardiovascular anomalies

Routine echocardiography is recommended to detect and grade the severity of cardiovascular anomalies. Infants with major cardiac anomalies have 30% risk of mortality.<sup>[11]</sup> Most common single cardiac defects; ventricular septal defect (VSD) carries 16% mortality risk. Over 87% VSD closes as the age advances. Congenital heart disease with high pulmonary flow rarely causes a problem in the immediate neonatal period because of the residual high pulmonary vascular resistance.

**Table 1: Reported incidence of associated anomalies in OA-TEF**

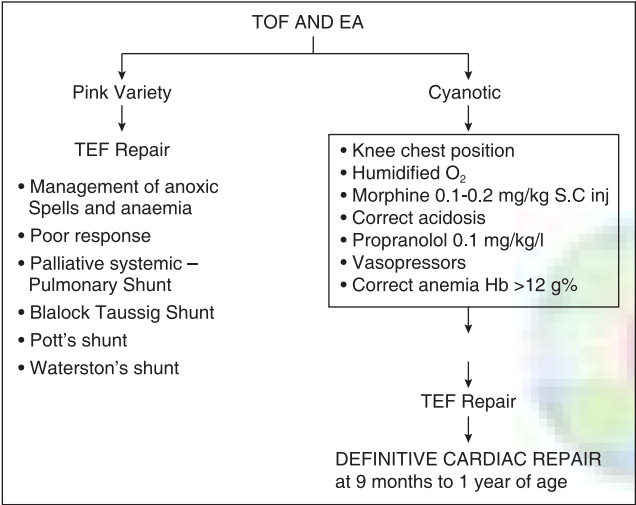
| Series                              | Total number of patients | Patient with congenital anomalies (%) | Type of abnormality |             |                 |                      |                 |                   |
|-------------------------------------|--------------------------|---------------------------------------|---------------------|-------------|-----------------|----------------------|-----------------|-------------------|
|                                     |                          |                                       | Cardiac (%)         | Urinary (%) | Orthopaedic (%) | Gastrointestinal (%) | Chromosomal (%) | Miscellaneous (%) |
| Holder <i>et al.</i> (1964)         | 1058                     | 52                                    | 19                  | 10.3        | 8.5             | 22                   | 2.6             | 20                |
| Holder <i>et al.</i> (1987)         | 100                      | >50                                   | 25                  | 8           | 15              | 15                   | 3               | —                 |
| Spitz <i>et al.</i> (1987)          | 148                      | 47                                    | 21.5                | 12.2        | 11              | 23                   | 2               | 14                |
| Chittimittapap <i>et al.</i> (1989) | 253                      | 48                                    | 29                  | 14          | 10              | 27                   | 4               | —                 |
| Ein <i>et al.</i> (1989)            | 97                       | 53                                    | 29                  | 8           | 12.3            | 17                   | 8               | 12                |
| Strodel <i>et al.</i> (1979)        | 365                      | 31.6                                  | 26                  | 16          | 15              | 25                   | —               | 18                |
| Louhimo (1983)                      | 500                      | 40.6                                  | 13.2                | 12          | 11              | 15.8                 | 3.2             | 12                |
| Lindahl (1983)                      | 200                      | 51                                    | 19.5                | 13.5        | 15.5            | 14.5                 | 4               | 19                |
| RCH (Melbourne) (1948-1968)         | 584                      | 58                                    | 20                  | 22          | 15.5            | 22.5                 | 4.8             | 18                |

<sup>a</sup>In some series genital anomalies have been included. OA: Oesophageal atresia; TEF: Tracheo-oesophageal fistula; RCH: Royal Children Hospital fact sheet

In patient with patent ductus arteriosus (PDA) dependent anomalies, infusion of prostaglandin E<sub>1</sub> may allow early oesophageal repair. Patients, who do not have improvement, may benefit from initial palliative or corrective cardiac surgery.<sup>[12]</sup>

Patent PDA in premature and low birth weight babies causing congestive heart failure usually respond to indomethacin therapy. Non-closure to medical therapy demands PDA ligation through left thoracotomy, pre- or post-TEF repair as the situation might warrant.

**Urgent of treatment is determined by the degree of cyanosis and hypoxia**



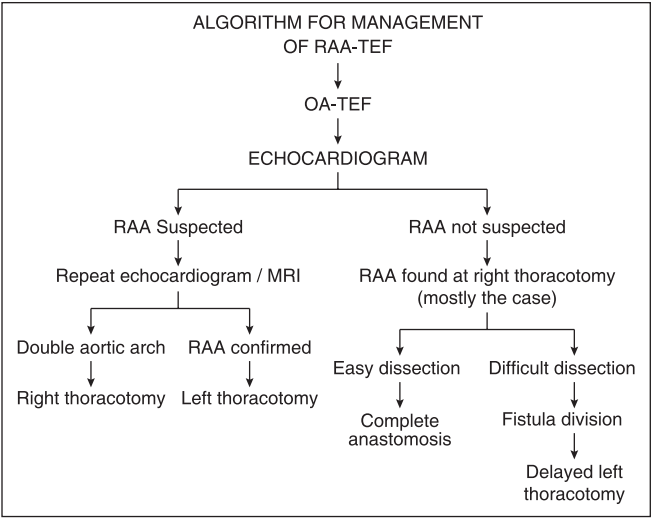
About 13-20% patients with tetralogy of Fallot are associated with right sided aortic arch which will have its own impact on TEF repair.

**Right aortic arch anomaly**

About 8% infants with OA have aortic arch anomalies.<sup>[13]</sup> About 5% infants with OA have right aortic arch (RAA).<sup>[14,15]</sup> Pre-operative detection rate by echocardiogram and chest X-ray is reported in up to 8-10%.<sup>[14,15]</sup> Magnetic resonance angiography and spiral computed tomography scan generally are not part of the routine pre-operative investigations. Three types of RAA have been described:<sup>[16-18]</sup>

1. Right aortic arch descending on right side or spine with mirror image branching of innominate and subclavian arteries
2. Solitary RAA passes over right main bronchus, then returns to left passing behind oesophagus to descend on the left side of vertebra
3. Double aortic arch.

Management of RAA is controversial.



**Table 2: “Significance” of the grading of associated anomalies in OA-TEF**

| Relevance of associated anomaly in OA-TEF                                | Examples                               |
|--------------------------------------------------------------------------|----------------------------------------|
| Not relevant in relation to management                                   | Meckle’s diverticulum, duplex kidney   |
| Relevant because of frequency of association (treatment may be required) | Vertebral anomalies                    |
| Demand treatment but not urgently and OA takes undisputed priority       | PUJ obstruction                        |
| Demand early treatment                                                   |                                        |
| Needs to be coordinated with treatment of OA                             | Duodenal atresia and anorectal anomaly |
| Does not need to be coordinated with treatment of OA                     | Congenital hip dislocation of the hip  |
| May take priority over complete repair of OA                             | PDA dependent congenital heart disease |
| Incompatible with long-term survival                                     | Trisomy 18 bilateral renal agenesis    |

OA: Oesophageal atresia; TEF: Tracheo-oesophageal fistula; PDA: Patent ductus arteriosus; PUJ: Pelvi-ureteric junction

**Table 3: Systemic distribution of associated anomalies in OA-TEF**

| System           | Percentage |
|------------------|------------|
| Cardiovascular   | 35         |
| Genitourinary    | 20         |
| Gastrointestinal | 24         |
| Anorectal        | 11.1       |
| Others           | 12.9       |
| Orthopaedics     | 13         |
| Vertebral        | 10         |
| Others           | 3          |
| Neurological     | 5.3        |
| Eye              | 11.1       |
| Chromosomal      | 5.3        |
| Miscellaneous    | 15.4       |

OA: Oesophageal atresia; TEF: Tracheo-oesophageal fistula

| Table 4: Comprehensive list of associated anomalies                                |                       |
|------------------------------------------------------------------------------------|-----------------------|
| System                                                                             | Percentage            |
| Cardiovascular anomalies                                                           | 30-35                 |
| VSD                                                                                | 35 most common        |
| Tetralogy of fallot                                                                | 13 second most common |
| PDA                                                                                | 11                    |
| ASD                                                                                | 11                    |
| RAA                                                                                | 5                     |
| Coarctation of aorta                                                               | 1-1.5                 |
| Others                                                                             |                       |
| Vascular ring                                                                      |                       |
| Single umbilical artery                                                            |                       |
| Patent foramen ovale                                                               |                       |
| Dextrocardia                                                                       |                       |
| Abnormal subclavian artery                                                         |                       |
| AVA                                                                                |                       |
| Complex cardiac anomalies, for example, total anomalies pulmonary vein connections |                       |
| Pulmonary atresia                                                                  |                       |
| Gastrointestinal anomalies                                                         | 15-24                 |
| Anorectal malformations                                                            | 11                    |
| High                                                                               | 47                    |
| Intermediate                                                                       | 3                     |
| Low                                                                                | 40                    |
| Cloacal                                                                            | 30                    |
| Pouch colon                                                                        | 2                     |
| Others                                                                             |                       |
| Duodenal and ileal atresia                                                         | 6-10                  |
| Malrotation                                                                        |                       |
| Pancreato-biliary                                                                  |                       |
| Distal oesophageal stenosis                                                        |                       |
| Meckel's diverticulum                                                              |                       |
| Omphalomesenteric duct cyst                                                        |                       |
| Genito urinary anomalies                                                           | 18-24                 |
| Hypospadias                                                                        |                       |
| Undescended testis                                                                 |                       |
| Renal agenesis or hypoplasia                                                       |                       |
| Cystic renal disease                                                               |                       |
| Hydronephrosis                                                                     |                       |
| Vesico-ureteric reflux                                                             |                       |
| PUJ and obstruction                                                                |                       |
| Urachal abnormality                                                                |                       |
| Ambiguous genitalia                                                                |                       |
| Cloacal or bladder exstrophy                                                       |                       |
| Musculoskeletal anomalies                                                          | 10-15                 |
| Vertebral                                                                          | 10                    |
| Fused vertebra                                                                     |                       |
| Hemivertebra                                                                       |                       |
| Others                                                                             |                       |
| Rib anomalies (13 pairs, fusion, agenesis)                                         |                       |
| Radial Amelia                                                                      |                       |
| Poly and syndactyly                                                                |                       |
| Pes varus                                                                          |                       |
| Congenital dislocation of hip                                                      |                       |
| Rocker bottom feet                                                                 |                       |
| Neurological anomalies                                                             | 5-10                  |
| Neural tube defects                                                                | 2.3                   |
| Hydrocephalus                                                                      | 5.2                   |
| Holoprosencephaly                                                                  | 2.3                   |

| Table 4: Continued                                                                                                |            |
|-------------------------------------------------------------------------------------------------------------------|------------|
| System                                                                                                            | Percentage |
| Others                                                                                                            |            |
| Vocal cord anomaly                                                                                                |            |
| Dilated 3 <sup>rd</sup> ventricle                                                                                 |            |
| Facial nerve anomaly                                                                                              |            |
| Vagal anomaly                                                                                                     |            |
| Olfactory nerve absence                                                                                           |            |
| Micro or megacephaly                                                                                              |            |
| Absent midbrain or cerebellum                                                                                     |            |
| Spastic extremities                                                                                               |            |
| Eye anomalies                                                                                                     | 1.5-2      |
| Anophthalmia                                                                                                      |            |
| Microphthalmia                                                                                                    |            |
| Chromosomal anomalies                                                                                             | 5-7        |
| Down's syndrome                                                                                                   |            |
| Trisomies 13, 18                                                                                                  |            |
| Associations: Only 1.5% TEF patients have full VATER and 17-25% has three components of VACTERL (1-4) association |            |
| VATER/VACTERL                                                                                                     |            |
| Vertebral defects                                                                                                 |            |
| Anal atresia                                                                                                      |            |
| Cardiac anomalies                                                                                                 |            |
| Tracheo-oesophageal fistula and atresia                                                                           |            |
| Radial and renal dysplasia                                                                                        |            |
| Limb anomalies                                                                                                    |            |
| Charge                                                                                                            |            |
| Coloboma                                                                                                          |            |
| Heart defects                                                                                                     |            |
| Atresia choanal                                                                                                   |            |
| Development retardation                                                                                           |            |
| Genital hypoplasia                                                                                                |            |
| Ear deformities (deafness)                                                                                        |            |
| Schisis                                                                                                           |            |
| Omphalocele                                                                                                       |            |
| Neural-tube defects                                                                                               |            |
| Cleft lip and palate                                                                                              |            |
| Genital hypoplasia                                                                                                |            |
| Craniofacial anomalies                                                                                            | 20-25      |
| Choanal stenosis or atresia                                                                                       |            |
| Ear deformity                                                                                                     |            |
| Pre-auricular skin tag                                                                                            |            |
| Micrognathia                                                                                                      |            |
| Macrostomia                                                                                                       |            |
| Facial hypoplasia                                                                                                 |            |
| Cleft lip and palate                                                                                              |            |
| Tracheobronchial thoraco pulmonary anomalies                                                                      |            |
| Tracheal agenesis                                                                                                 |            |
| Laryngeal atresia                                                                                                 |            |
| Laryngo tracheal cleft                                                                                            |            |
| Pulmonary agenesis                                                                                                |            |
| Cystic adenomatoid malformations                                                                                  |            |
| Diaphragmatic hernia                                                                                              |            |
| Tracheomalacia                                                                                                    |            |
| Subglottic stenosis                                                                                               |            |
| Syndromes associated with OA                                                                                      |            |
| Down syndrome                                                                                                     |            |
| Fanconi's syndrome                                                                                                |            |
| Townes-Brocks syndrome                                                                                            |            |

**Table 4: Continued**

| System                          | Percentage |
|---------------------------------|------------|
| Bartsocas–Papavasiliou syndrome |            |
| McKusick–Kaufmann syndrome      |            |
| Potter's syndrome               |            |
| Goldenhar syndrome              |            |

VSD: Ventricular septal defect; PDA: Patent ductus arteriosus; ASD: Atrial septal defect; RAA: Right sided aortic arch; AVA: Azygos vein anomaly; PUJ: Pelvi-ureteric junction; TEF: Tracheo-oesophageal fistula; OA: Oesophageal atresia

A strong correlation has also been described between RAA, long gap atresia and vascular atresia anomalies.<sup>[13]</sup> These infants have five folds increase in major postoperative complications including leak and stricture.<sup>[18,19]</sup> Canty *et al.*<sup>[13]</sup> reported high incidence of aberrant left subclavian arteries in infants with long gap (>3 cm) OA-TEF and RAA, requiring left thoracotomy for definitive repair of both the anomalies.

- Infants with OA cardiac anomalies should be immediately put on prophylactic antibiotics to prevent infective endocarditis.
- Cases with severe coarctation of aorta with poor distal perfusion, a less invasive balloon angioplasty is performed prior to OA-TEF repair.
- Recently, authors have described various types of azygos vein anomalies in association with TEF. The presence of anomalous azygos vein denotes a wide gap OA, small upper pouch and the possibility of a upper pouch fistula.<sup>[20]</sup>

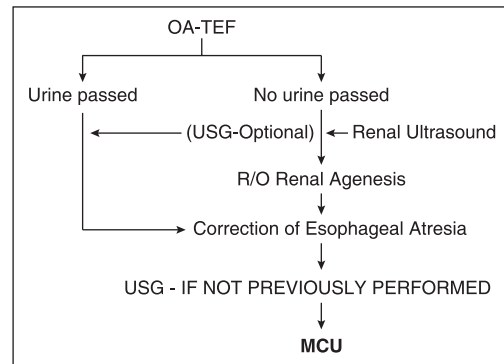
### Gastrointestinal anomalies

Pure OA has higher incidence (30%) of anorectal malformations when compared to those with OA and TEF (1%).<sup>[4]</sup> Incidence of various types of anorectal malformations and the type of OA are shown in Table 5.<sup>[21]</sup> Non-anorectal gastrointestinal anomalies occur in 6-10% of cases of OA-TEF have been shown in Table 4.

Oesophageal stenosis is a rare association more commonly found in patients with H type of TEF. A regular practice of probing the distal pouch during the surgical repair of all cases of OA-TEF and the H type in particular, would diagnose such problems early. If detected, demands diversion in the form of an oesophagostomy and a gastrostomy.

### Genitourinary anomalies

Algorithm for investigation of urinary tract in infants with OA-TEF



Beasley *et al.*<sup>[22]</sup> classified urinary abnormalities in four groups according to their impact on the need for management [Table 6].

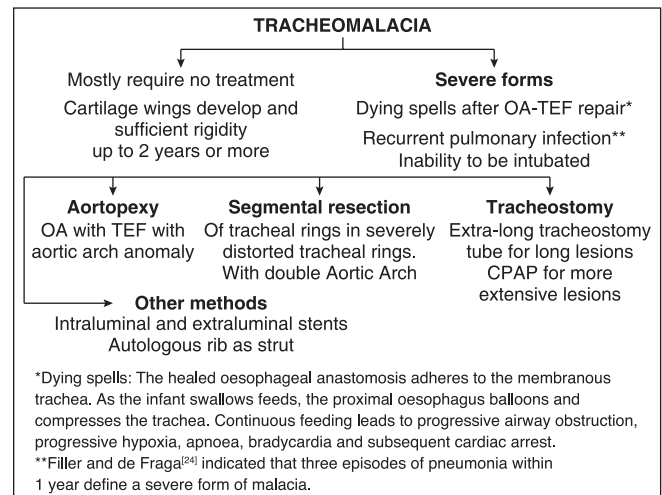
It is important to recognise that many patients with bilateral renal agenesis do not have features suggestive of Potter's syndrome in the presence of OA probably because the oligohydramnios of renal agenesis is counteracted by the tendency to polyhydramnios with OA. It is thus unlikely that these patients can be identified pre-operatively on clinical grounds alone.

### Respiratory system anomalies

#### Tracheomalacia

A unique form of tracheomalacia is associated with TEF.<sup>[23,24]</sup> The lumen of trachea in the vicinity of fistula (TEF) has a crescent or D-shaped configuration because of an abnormally wide membranous portion of the trachea. The area of TEF is most affected, and the anomalous membranous trachea may extend to a varying distance proximally and involve the bronchi distally. These infants and children have a peculiar barking cough and expiratory stridor, which is prominent than in infants with other forms of malacia.

#### Algorithm of management of tracheomalacia



**Table 5: Association between types of anorectal malformations and types OA**

| Types of OA                                   | Type of anorectal malformations |              |         |         | Total number | Percentage anorectal malformation with each type of OA |
|-----------------------------------------------|---------------------------------|--------------|---------|---------|--------------|--------------------------------------------------------|
|                                               | High                            | Intermediate | Low     | Cloacal |              |                                                        |
| OA with distal TEF (type C)                   | 11                              | 0            | 10      | 2       | 23           | 11                                                     |
| OA with proximal TEF (type B)                 | 0                               | 0            | 0       | 0       | 0            | 0                                                      |
| OA with both proximal and distal TEF (type D) | 1                               | 0            | 0       | 0       | 1            | 11                                                     |
| Isolated OA (type A)                          | 2                               | 1            | 2       | 1       | 6            | 30                                                     |
| H type TEF without OA (type E)                | 0                               | 0            | 0       | 0       | 0            | 0                                                      |
| Total number (%)                              | 14 (47)                         | 1 (3)        | 12 (40) | 3 (10)  | 30 (100)     |                                                        |

TEF: Tracheo-oesophageal fistula; OA: Oesophageal atresia

**Table 6: Urological anomalies associated with OA-TEF**

| Groups    | Type of anomalies                                                                                                                                                                                                     |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Group I   | Abnormalities of no clinical significance<br>Horseshoe kidney<br>Ureteric duplication<br>Crossed ectopia<br>Malrotation<br>Duplication                                                                                |
| Group II  | Abnormalities likely to require no immediate treatment but may become significant later in life<br>Unilateral renal agenesis<br>Unilateral hypoplasia<br>Pelvic kidney<br>Renal cyst<br>MCKD<br>Malrotation<br>Duplex |
| Group III | Abnormalities likely to require treatment (medical/surgical)<br>VUR (54%) <sup>[22]</sup><br>PUJ obstruction<br>VUJ<br>Diverticulum<br>Ectopic ureter<br>Double urethra<br>Renal scars-(5%)<br>Megaureter             |
| Group IV  | Abnormalities likely to lead to early failure or death.<br>OA-TEF repair is contraindicated in the Group IV anomalies (3% of cases)<br>Bilateral renal agenesis<br>Bilateral renal dysplasia                          |

TEF: Tracheo-oesophageal fistula; OA: Oesophageal atresia; MCKD: Multi-cystic dysplastic kidney; VUR: Vesico-ureteric reflux; PUJ: Pelvi-ureteric junction; VUJ: Vesico-ureteric junction

### Pulmonary agenesis

Only 33 cases have so far been reported since 1874.<sup>[25]</sup> These are uniformly lethal anomalies affecting mostly right lung with right main bronchus being replaced by the distal oesophagus. More than 50% have VATER association and/or heart defects. About 50% children are stillborn or else die within the first few months of the life from the concomitant anomalies. Survivors of OA-pulmonary aplasia carry poor survival due to recurrent respiratory infection and failure of solitary lung.

### Laryngo tracheoesophageal cleft (symptomatic types II, III, and IV)

Subglottic stenosis, tracheal stenosis, laryngeal atresia require bronchoscopic evaluation of early tracheostomy prior to the repair of OA-TEF. Definitive (tracheo/laryngoplasty) of individual defects is undertaken at a later date.

### Congenital diaphragmatic hernia and oesophageal atresia-tracheoesophageal fistula

Only seven cases have been reported till date since the first case of the rare association was reported by Ahmed.<sup>[26-29]</sup> The respiratory distress is usually severe. Each case needs to be individualised depending on the severity of the disease. A pre-operative stabilization is important before repairing the diaphragmatic defect. Both the defects can be repaired simultaneously. However, in babies with severe chest infection, only fistula ligation may be considered as the initial step to prevent reflux pneumonitis.

### CONCLUSION

Associated anomalies of OA and TEF require comprehensive assessment and uniform documentation. Cognizance of above mentioned issues would enable quick and overall assessment of a child with TEF, better timing of interventions, accurate prognostication and realistic counselling of parents so as to adjust their understanding and expectations.

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