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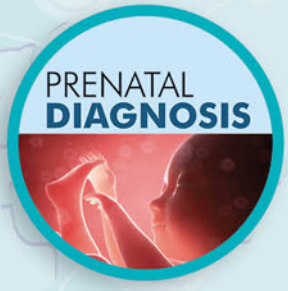


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# Esophageal atresia in twins compared to singletons: In utero manifestation and characteristics

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## Abstract

**Objective:** Esophageal atresia with/without tracheo-esophageal fistula (EA/TEF) is more common among twins. The detection of polyhydramnios might be altered in twins, leading to EA/TEF underdiagnosis, prenatally. The aim of the study was to compare the prenatal manifestation of EA/TEF between twins and singletons.

**Methods:** A 12-year study of EA/TEF cases was performed at a tertiary center. Cases exhibiting (a) small/absent stomach or (b) polyhydramnios were considered **"suspected"**; cases with (c) esophageal pouch were considered **"detected."** We compared the rate and timing of appearance of these signs between the groups.

**Results:** There were 76 cases of EA/TEF, of which 17 were a co-twin. All twin pairs were EA/TEF discordant. The prevalence of EA/TEF at our center was 1:750 for twins (1:319 monochorionic and 1:1133 dichorionic) and 1:2399 for singletons. The rate of small/absent stomach, polyhydramnios and pouch in twins vs singletons was 23.5%, 47.1%, 29.4% and 39.7%, 72.4%,34.5%, respectively ($P$ = .2, $P$ = .09 and $P$ = .7). Esophageal pouch was detected earlier in twins (***P* = .03**). Twins were scanned more frequently (×1.8 times, ***P* = .01**).

**Conclusion:** EA/TEF is more prevalent in twins. Despite lower rate of polyhydramnios, twins were similarly detected prenatally as singletons, and this was accomplished earlier in pregnancy; perhaps reflecting more frequent scans.

## 1 | INTRODUCTION

Esophageal Atresia with or without Tracheo-esophageal Fistula (EA/TEF) occurs in 2.3-2.4 out of 10 000 births.[1,2]

Approximately one third of fetuses with EA/TEF are diagnosed prenatally[1,3] . Prenatal detection relies on three sonographic clues: polyhydramnios, absent or small stomach bubble and an esophageal pouch—the dilated blind-end of the upper esophageal segment.[4,5] While, polyhydramnios and small/absent stomach bubble are not highly specific for the diagnosis of EA/TEF and can be found in a variety of different conditions,[6-10] an esophageal pouch, when identified correctly, is diagnostic of EA with a reported 100% positive predictive value.[5,11-13] Fetal MRI has been found to further improve the diagnostic accuracy of EA/TEF.[14-17]

Compared to singletons, twin pregnancies have a higher rate of EA/TEF,[18,19] necessitating a higher index of suspicion when scanning twins. Polyhydramnios is the most common indirect sign of EA,[3] making it an important indication to scan for EA/TEF. However, there are factors that might affect the perception and attitude towards polyhydramnios in multiple pregnancies.[20,21] First of all, the presence of two gestational sacs in one cavity could affect our subjective estimation and quantitive measurement of amniotic fluid volume[20] . Secondly, as the most common etiology for polyhydramnios in monochorionic pregnancy is twin to twin transfusion syndrome,[22] this

Tal Weissbach and Eran Kassif should be considered joint first authors

might lead clinicians to overlook EA as a possible diagnosis. These factors could potentially lead to an underdiagnosis of EA/TEF in twins.

The primary aim of our study was to compare the rate of sonographic signs and prenatal detection of EA/TEF between singletons and twins. Our secondary aim was to compare the same parameters between monochorionic and dichorionic twins.

Materials and Methods: This was a retrospective study on the prenatal diagnosis of EA/TEF in multiple vs singleton pregnancies performed at a single tertiary center, between 2006 and 2019. This study is a subgroup analysis of a dataset previously analyzed and assessed for the manifestation of EA/TEF throughout pregnancy.[23] In the current study, the prenatal course of multiple and singleton pregnancies, was assessed for the rate and timing of detection of the three manifesting signs of EA/TEF- polyhydramnios (maximal vertical pocket -MVP ≥8 cm or amniotic fluid index -AFI ≥24 cm; severe polyhydramnios was considered at MVP ≥16 cm or AFI ≥35 cm)[24,25] and small/absent stomach (stomach dimensions were either measured and compared to a size chart[26] and in some cases subjectively determined to be small by the sonographer), which are indirect signs and were considered **suspicious**, and an esophageal pouch (Figure 1), which is a direct sign of EA and was considered **diagnostic**. Postnatally, all liveborn cases were diagnosed on chest x-ray with contrast media. We counted the number of focused and routine anomaly scans performed in each case until the diagnosis of a pouch was reached or until delivery, in cases where a pouch was not detected.

Additional characteristics compared between the groups were whether the EA/TEF was isolated, associated with VACTERL (2 or more of the following anomalies: Vertebrae, Anal atresia, Cardiac, Tracheo-Esophageal atresia, Renal and Limbs) or accompanied by other non-VACTERL anomalies (termed as "other multiple anomalies"). Genetic results were classified as clinically significant, if they were known to be of clinical significance, or nonsignificant, if they were regarded as a variant of unknown significance, by genetic counsellors.

We reviewed medical records including ultrasound reports and images, MRI reports, genetic and laboratory workup, obstetric clinic visits, labor ward reports and neonatal intensive care unit (NICU) reports both in twins and singletons. Description of chorionicity of twin pregnancies was mandatory only from 2010; therefore, epidemiological data comparing dichorionic (DC) vs monochorionic (MC) twins are based on deliveries 2010–2019 (87% of all twins in the study).

The study protocol was approved by the Institutional Ethics Committee at Chaim Sheba Medical Center (approval number 5238-18-SMC).

### What's already known about this topic?

- There is an over representation of twins in the esophageal atresia population. Yet, an actual prevalence has never been previously published.

### What does this study add?

- Esophageal atresia is 3.2 more common among twins (1:750 twin births), especially among monochorionic twins (7.6 OR).
- Affected twins are more likely to be free of sonographic signs compared to singletons.
- Both groups have similar prenatal detection rates of about 30%.
- Esophageal atresia is highly associated with VACTERL sequence in monochorionic twins.

## 1.1 | Statistical analysis

Normality of the data was tested using the Shapiro-Wilk or Kolmogorov-Smirnov tests. Data are presented as median and interquartile range (IQR). Comparison between unrelated variables was

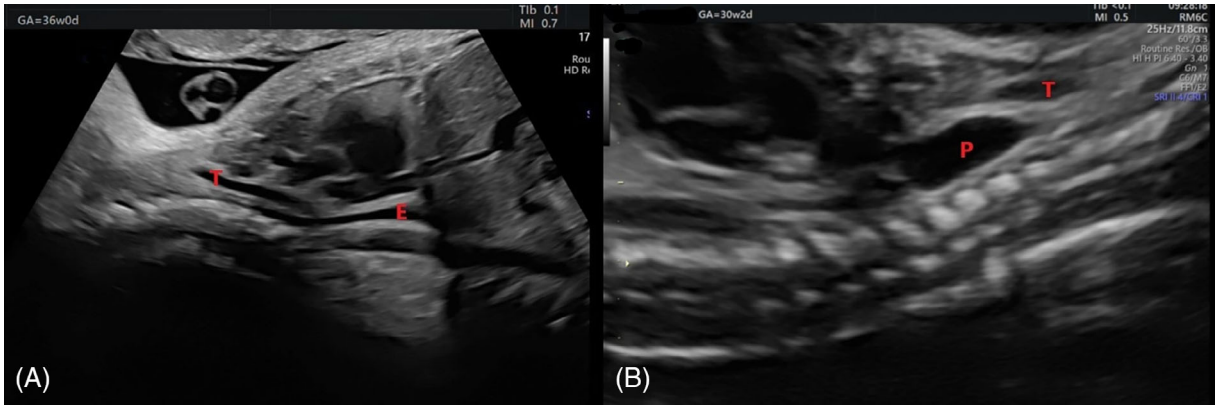


**FIGURE 1** Esophagus assessment. A, A patent fluid filled esophagus (E) during fetal swallowing. Located posterior to the trachea (T) in the neck and upper chest and posterior to the heart in the lower chest. B, An esophageal pouch (P) reaching the level of the aortic arch in a case of esophageal atresia [Colour figure can be viewed at wileyonlinelibrary.com]

conducted with Student's *t* test or Mann-Whitney *U* test, as appropriate. The $\chi^2$ and Fisher's exact tests were used for comparison between categorical variables. Significance was accepted at $P < .05$. Statistical analyses were conducted using the IBM Statistical Package for the Social Sciences (IBM SPSS v.23; IBM Corporation Inc, Armonk, New York).

## 2 | RESULTS

Over a 12-year period, a total of 76 cases were diagnosed with EA/TEF, either prenatally (n = 25) or postnatally (n = 51). The group consisted of 59 singletons and 17 twin pregnancies (9 Dichorionic (DC) twin pregnancies and 8 Monochorionic Diamniotic (MC/DA) twin pregnancies). Seventy-one cases were liveborn, with a postnatal diagnosis of the type of EA/TEF, while 5 other cases ended with an intrauterine fetal demise (IUFD; n = 2) or termination of pregnancy (TOP; n = 3). During the period of the study, there was a total of 141 525 singleton and 12 748 twin births at our center. Twins had significantly ($P < .001$) higher rates of EA/TEF compared to singletons (1:2399 in singletons vs 1:750 in twins; LR = 3.2, 95%CI = 1.87-5.49) and MC twins had significantly higher rates of EA/TEF (1:319) compared to singletons and DC twins (LR = 7.68; 95%CI = 3.64-14.49, $P < .001$ and LR = 2.3, 95%CI = 1.16-3.49,$P = .013$, respectively) .

One of the 76 cases did not undergo ultrasound scans during the pregnancy and therefore was only included in the maternal demographics and peri/postnatal data analysis. Altogether there were 75 patients in our series that were prenatally scanned. Demographics and clinical characteristics of both groups are presented in Table 1. No statistically significant differences were observed in maternal demographics between the groups.

### 2.1 | The prenatal diagnosis of EA/TEF in multiple vs singleton pregnancies

Table 2 compares the detection rate of the three manifesting signs and the timing of their appearance, between the groups. There was a higher rate of absent sonographic signs in twin pregnancies compared to singletons, at borderline significance, making twins with EA/TEF less detectable. The most common indirect sign of EA/TEF in both groups was polyhydramnios, but it was more common among singletons, at a borderline significance. Moreover, **severe** polyhydramnios was also more common in singletons affected by EA/TEF. Multiple pregnancies had more prenatal scans compared to singletons ($P = .01$).

Figure 1 addresses the timing of appearance of the three prenatal imaging signs. Esophageal pouch was diagnosed earlier in twins compared to singletons, at a median gestational age of 28 vs 33 weeks, respectively. This difference was statistically significant ($P = .03$). An earlier detection of polyhydramnios and small/absent stomach among twins was not statistically significant; ($P = .3$ and .1, respectively).

There were no statistically significant differences in associated anomalies and genetic abnormalities between the groups (Table 3). However, there are some trends to point out. Twins were more associated with VACTERL than their singleton peers. None of the twins genetically evaluated were found to have an aberration, compared to 10% clinically significant chromosomal abnormalities in the singleton group. There was a similar distribution of TEF types between the groups, with the majority being type C in both groups. Interestingly, the six cases of type A (pure EA) were exclusively found in the singleton group.

Table 4 compares the perinatal outcome of both groups. There was a similar livebirth rate between the groups. There were two cases of IUFD and two TOPs in the singleton group. One monochorionic pregnancy was selectively terminated. Twins were born at an earlier gestational age and at lower birthweights. However, there were not statistically significant differences in the rate of intrauterine growth restriction (IUGR) between the groups. Neonates in both groups had surgical repair at around day 3 of life. There was a similar postnatal death rate among the groups. Singletons with EA/TEF were predominantly male while twins were predominantly female.

### 2.2 | The prenatal diagnosis of EA/TEF in monochorionic vs dichorionic twins

Table 5 compares the rate of detection of all three sonographic features of EA/TEF, as well as the absence of features on ultrasound, between mono- and dichorionic twin pregnancies. The rate of sonographic signs was comparable between the groups with up to 33% prenatal EA/TEF diagnosis (pouch) and around half of cases prenatally

**TABLE 1** Demographics and clinical characteristics of study groups

| | Singleton (N = 59) | Twins (N = 17) | *P* value |
|---|---|---|---|
| Maternal age | 32 (28-36) | 33 (28.5-34) | .7 |
| Nulliparity | 35.6% (21/59) | 41.2% (7/17) | .67 |
| IVF pregnancy | 16.9% (10/59) | 23.5% (4/17) | .5 |
| Pre-pregnancy BMI | 24 (21-27.8) | 24.1 (20.5-31.1) | .87 |
| Pre-pregnancy BMI ≥30 | 25.6% (11/43) | 28.6% (4/14) | 1 |
| Pregnancy weight gain | 11.8 (8-15.75) | 11 (5.5-20.5) | .76 |

*Note:* Data presented as percentage or median and IQR.

**TABLE 2** Detection rate of the three sonographic features of TEF/EA

| Signs | Singleton (N = 58) | Twins (N = 17) | *P* value |
|---|---|---|---|
| Polyhydramnios | 72.4% (42/58) | 47.1% (8/17) | .09 |
| Severe Polyhydramnios | 36.2% (21/58) | 11.6% (2/17) | .05 |
| Small/Absent Stomach | 39.7% (23/58) | 23.5% (4/17) | .2 |
| Esophageal Pouch | 34.5%[a] (20/58) | 29.4% (5/17) | .7 |
| Absent Sonographic Signs | 25.9% (15/58) | 47.1% (8/17) | .09 |
| Number of Scans Performed | 3 (2–4) | 4 (3–7) | .01 |

*Note:* Data presented as percentage or median and IQR.
[a]Three cases detected on MRI.

**TABLE 3** Distribution of associated anomalies, genetic abnormalities and TEF types among groups

| | Singleton (N = 59) | Twins (N = 17) | *P* value |
|---|---|---|---|
| Isolated EA | 42.4% (25/59) | 29.4% (5/17) | .33 |
| VACTERL association | 49.1% (29/59) | 64.7% (11/17) | .28 |
| Other multiple anomaly | 8.5% (5/59) | 5.9% (1/17) | .65 |
| Type of EA[a] | | | |
| A | 10.9% (6/55) | 0% (0/16) | .17 |
| B | 0% (0/55) | 6.6% (1/16) | |
| C | 85.5% (47/55) | 87.5% (14/16) | |
| D | 1.8% (1/55) | 0% (0/16) | |
| E | 1.9% (1/55) | 6.7% (1/16) | |
| Aneuploidy | 2/31 (6.5%) | 0% (0/10) | 1 |
| Copy number variant | 26.7% (4/15) | 0% (0/6) | .28 |
| Clinically significant chromosomal abnormality | 9.7% (3/31) | 0% (0/10) | .56 |

[a]Five IUFD and TOP cases are of undetermined types.

**TABLE 4** Perinatal outcomes—twins vs singletons

| | Singleton (N = 59) | Twins (N = 17) | *P* value |
|---|---|---|---|
| Termination of pregnancy | 3.4% (2/59) | 5.9% (1/17) | .54 |
| Stillbirth | 3.4% (2/59) | 0% (0/17) | 1 |
| Livebirth | 93.2% (55/59) | 94.1% (16/17) | 1 |
| Gestational age at delivery | 37.4 (35-39) | 34.4 (32.6-36.2) | .001 |
| Birth weight (gr) | 2580 (2115-2910) | 1633 (1340-2051) | <.001 |
| IUGR | 39% (23/59) | 41.2% (7/17) | .87 |
| Male gender | 67.8% (40/59) | 41.2% (7/17) | .04 |
| Age at EA repair (days) | 3 (2–6) | 3 (3–4) | .33 |
| Postnatal death | 9.1% (5/55) | 6.3% (1/16) | 1 |

*Note:* Data presented as percentage or median and IQR.

undetectable (absent signs). Monochorionic twins were significantly scanned more. Of the three monochorionic twins that developed polyhydramnios, none were associated with twin to twin transfusion syndrome.

Data regarding associated malformations and genetic abnormalities is presented in Table 6. There was a similar distribution of the types, most being type C. None of the monochorionic cases were isolated, in fact, all of them were part of VACTERL association. More than half of the dichorionic twins were isolated, a third were part of VACTERL and one case was associated with other anomalies. Neither of the groups had accompanying chromosomal abnormalities.

## 3 | DISCUSSION

This is the first study to address the comparison of the prenatal manifestation of EA/TEF between twins and singletons, and furthermore, between monochorionic and dichorionic pregnancies. The literature is mostly comprised of various case reports[27-30] and a few

**TABLE 5** The detection rate of sonographic features between monochorionic and dichorionic pregnancies

| Signs | Monochorionic (N = 8) | Dichorionic (N = 9) | *P* value |
|---|---|---|---|
| Polyhydramnios | 37.5% (3/8) | 55% (4/9) | .67 |
| Severe Polyhydramnios | 0% (0/8) | 22.2% (2/9) | .47 |
| Small/Absent Stomach | 25% (2/8) | 22.2% (2/9) | 1 |
| Esophageal Pouch | 25% (2/8) | 33.3% (3/9) | 1 |
| Absent Sonographic Signs | 50% (4/8) | 44.4$% (4/9) | 1 |
| Number of Scans Performed | 7 (3-10) | 3 (2.5-5) | .05 |

*Note:* Data presented as percentage or median and IQR.

**TABLE 6** Distribution of associated anomalies, genetic abnormalities and TEF types between monochorionic and dichorionic pregnancies

| | Monochorionic (N = 8) | Dichorionic (N = 9) | *P* value |
|---|---|---|---|
| Isolated EA | 0% (0/8) | 55.6% (5/9) | .03 |
| VACTERL association | 100% (8/8) | 33.3% (3/9) | .009 |
| Other multiple anomaly | 0% (0/8) | 11.1% (1/9) | 1 |
| IUGR | 62.5% (5/8) | 22.2% (2/9) | .15 |
| TEF type | | | |
| B | 12.5% (1/8) | 0% (0/8)[a] | .37 |
| C | 87.5% (7/8) | 87.5% (7/8)[a] | |
| E | 0% (0/7) | 12.5% (1/8)[a] | |
| Aneuploidy | 0% (0/4) | 0% (0/6) | - |
| Copy number variant | 0% (0/3) | 0% (0/3) | - |

[a]One case selective termination, type not determined.

epidemiologic studies with little reference to twins.[31] The only two existing articles on EA/TEF in twins address aspects other than prenatal diagnosis; One studied the concordance rate of EA/TEF in twins[32] and the other studied possible underlying mechanisms for the development of EA/TEF in twins.[18]

## 3.1 | The prevalence of EA/TEF in twins

Our series was comprised of 22.4% twins and 77.6% singletons. We calculated a prevalence of EA/TEF of 1:750 among our twin population, (1:319 monochorionic and 1:1133 dichorionic, $P = .013$) and 1:2399 among our singleton population with a likelihood ratio of 3.2 (95% CI = 1.87-5.49). This extremely high prevalence among twins implies that twinning should be considered a risk factor for this anomaly. This association has been previously noted[31,32], but this is the first study to calculate EA/TEF prevalence in twins. Our study population is biased. The prevalence of twin pregnancies at our center is high, at around 4.3%. This could be due to our center's leading fetal medicine unit with a dedicated monochorionic clinic that receives nationwide referrals. Although our center has a large IVF unit, potentially contributing to the increased rate of twinning, our study group consists of 23.5% IVF conceived twin pregnancies, which is similar to that reported in the literature.[33]

The prevalence of EA/TEF in our singleton population was higher than that reported in the literature.[1,2] Perhaps this is due to higher rates of in vitro fertilization (IVF) pregnancies in our series (16.9% of singletons) compared to the general population,[34] as IVF is associated with a higher prevalence of congenital anomalies, in general.[35] In contrast, our IVF rate among twins was similar to that reported in the literature.[33] Therefore, we assume that IVF did not create a bias effect on the prevalence of EA/TEF among twins.

## 3.2 | The prenatal diagnosis of EA/TEF in twins compared to singletons

Our data exhibits a trend for lower rates of EA/TEF suspicion among twins (Table 2). Polyhydramnios was less detected in this group. Moreover, there was a difference in the rate of severe polyhydramnios between the groups, with singletons affected more than twins. Twins had a higher proportion of cases that were absent of sonographic signs, making them prenatally undetectable. Whether these signs develop less in twins or are less noticed, is beyond the scope of this study and should be assessed prospectively. As earlier mentioned, a difference in the assessment and perception of the amniotic fluid volume between singleton and multiple pregnancies[20,21] could potentially lead to underdiagnosis of polyhydramnios in this group.

Despite the lower rate of suspicion, esophageal pouches were detected earlier among twins (Figure 2). The earlier gestational age at detection could be the result of more frequent ultrasound scans, with approximately 1.8 times more scans on average in twins.


**FIGURE 2** Gestational age of the three sonographic signs of TEF/EA in singleton and twin pregnancies (median ± IQR) [Colour figure can be viewed at wileyonlinelibrary.com]

As this is the first study to compare the prenatal diagnosis of EA/TEF between twins and singleton, we can only compare our data to previous studies which have assessed prenatal diagnosis of EA/TEF in the general fetal population. Contrary to our study, most previous studies did not require the demonstration of an esophageal pouch as a criterion for the prenatal diagnosis of EA/TEF, but rather regarded a persistently small/absent stomach accompanied by polyhydramnios, equally diagnostic.[3,12,36-38] This approach has been shown to be inaccurate. Previous studies show that only a third of fetuses exhibiting a small/absent stomach **with** polyhydramnios and up to 10% cases of small/absent stomachs **without** polyhydramnios, have EA/TEF.[8,10] The rest are either normal or have other underlying entities such as neuromuscular abnormalities, pharyngeal obstruction.[7-10] Therefore, it is imprecise to discuss the performance of ultrasound in detecting EA/TEF in studies that have considered indirect signs as diagnostic. A few previous studies have specified the detection rate of an esophageal pouch.[5,39,40] These studies were small and did not distinguish singleton from multiple pregnancies. In two of these studies there was a reported pouch detection rate of about 25%,[5,40] which was similar to the detection rate found in our study. Only one of these studies evaluated the rate of all three sonographic signs in a cohort of fetuses that were postnatally confirmed to have EA/TEF.[39] In this study, by Brantberg et al, the reported rates of polyhydramnios, a small/absent stomach and pouch were 41.67%, 43.75% and 18.75%. Compared to this study, our data showed higher rates of polyhydramnios in both groups (72.4% and 47.1%) and similar rates of small/absent stomach in the singleton group, but lower rates in twins (39.7% and 23.5%). Our study displayed a higher detection rate of esophageal pouch in both of the groups (34.5% and 29.4%). The study by Brantberg et al did not elaborate on the distribution of the types of EA/TEF, which is important information when discussing differences in the rate of sonographic signs between the groups. The trend of higher rates of indirect sonographic signs among singletons in our study could be partially explained by the fact that all type A (pure EA) cases were singletons and, therefore, these cases displayed both absent stomach and polyhydramnios. Our pouch detection was better than that reported in this study, taking into account three singleton cases that were detected by MRI only. Moreover, we hypothesize that the rate of pouch detection is directly influenced by the degree of EA suspicion and the effort made to visualize fluid propagated in the esophagus during swallowing.[5]

### 3.3 | TEF type distribution, associated anomalies and other characteristics

Both groups had a similar distribution of EA/TEF types with type C being predominant in both groups, this is in agreement to previous studies of the general EA/TEF population.[15,36,37] What was found unique was that all six type A EA were exclusively found in the singleton group. The rate of additional anomalies in twins was similar to singletons and comparable to the literature.[1,15,36,37] Gender distribution was surprisingly different compared to singletons. Previous studies have found a male predominance among EA/TEF,[1,31,41] this is similar to what was found in the singleton study group (2.1:1), yet among twins there was a female predominance (1.4:1).

### 3.4 | Short term perinatal outcome

As expected, twins were born earlier and at lower birthweights. Yet, there was no difference in the rate of IUGR and in the short-term postnatal sequel among the groups. Despite being born earlier and smaller, both groups underwent surgical correction most commonly on day 3 and had similar, low rates of neonatal death. In our series, 8.4% (6/71) neonates died before discharge, one was a twin and the remainder, singletons. All postnatal deaths had associated cardiac anomalies and half of the cases were born under 1500 g, both of which are known risk factors for neonatal death among EA/TEF affected babies.[42] Our postnatal death rate is similar to that reported in the literature.[36]

### 3.5 | The prenatal diagnosis of EA/TEF in monochorionic vs dichorionic twins

The comparison of characteristics and prenatal diagnosis of EA/TEF between mono- and dichorionic twins has never been previously

studied. Therefore, there is no existing literature to address. A comparison in our series showed no significant differences in the rate of indirect or direct signs of EA/TEF between monochorionic and dichorionic twins (Table 5). Due to small numbers, the comparison of the gestational age at the time of sonographic sign presentation was limited.

A novel and intriguing observation was that monochorionic twins were 7.6 and 2.3 times more likely to be affected by EA/TEF, compared to singleton and dichorionic peers. The prevalence of EA/TEF among MC twins was calculated to be around 1:319, higher than that found in DC twins and singletons. Rendering monochorionicity a significant risk factor for EA/TEF. Another, interesting observation was that none of the monochorionic twins had isolated EA/TEF. In fact, all eight monochorionic twin cases were part of VACTERL association, while in dichorionic twins and singletons, there was a VACTERL association in 33% and 49%, respectively. Perhaps this significant VACTREL association among monochorionic twins points out a unique pathogenic mechanism of this group. We advocate that when a VACTERL associated anomaly is identified in a monochorionic twin, this should raise suspicion for co-existing EA/TEF and vice versa.

As for concordance rate, our data is not in agreement with a previous twin study that showed a 50% concordance among monochorionic twins and 26% among dichorionic twins.[32] All 9 dichorionic and 8 monochorionic twins were discordant for EA/TEF. This is in agreement with a large epidemiology study that included 18 pairs of twins (without mention of chorionicity), of which only 1 pair was concordant for EA.[31]

### 3.6 | Strengths and Weaknesses

Our study is limited by its retrospective nature. In some cases of reported small/absent stomach, we are not aware of whether this was a subjective perception, or the stomach bubble was actually measured and compared to a stomach size chart. To try to overcome this uncertainty, we retrospectively measured the stomach bubble on the abdominal circumference plane and compared it to a stomach size chart.[26] In most, but not all cases of polyhydramnios, was an amniotic fluid index reported, but rather commented normal/abnormal. A prospective study that collects real-time parameter indices, would overcome shortcomings of this nature. Another weakness of the study is a relatively small group of 17 sets of twins out of 76 cases, which accumulated over 12 years. This is due to the rarity of the condition.

The strengths of the study are, firstly, its precedence as the first study to assess this subject and secondly, its meticulous and high-resolution data collection from computerized charts, providing a wealth of information on a wide array of aspects related to esophageal atresia in mono and dichorionic twins.

### 3.7 | Future studies

In order to accurately assess the performance of prenatal ultrasound in detecting indirect and direct signs of esophageal atresia in twins and in singletons, a multicenter prospective study should be carried out with a uniform protocol of amniotic fluid index, stomach measurement and esophageal patency assessment.

## 4 | CONCLUSION

Twins have a higher prevalence of EA/TEF compared to singletons, 1:750 vs 1:2399. Twin pregnancy and especially MC twins are a significant risk factor for this entity. Twins affected by EA/TEF had lower rates of polyhydramnios, especially severe polyhydramnios, and a higher rate of absent sonographic signs. Despite lower rates of prenatal suspicion among twins, both groups had a similar rate of pouch detection, around 30%. Pouches were detected earlier among twins, perhaps reflecting more frequent scans in this group. Neonatal outcomes were similar for both groups.

Monochorionic twins diagnosed with a VACTERL associated anomaly should be scanned for co-existing EA/TEF.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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