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Review Article

Conjoined twins detected in the first trimester: A review

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Abstract

Conjoined twinning occurs in 1 in 100 sets of monozygotic twins, 1 in 50,000 gestations or 1 in 250,000 live births. With the advent of ultrasound technology, prenatal diagnosis of conjoined twins is possible. This article provides a comprehensive review of conjoined twins detected in the first trimester including fetal gender, maternal age, parity, types of fusion, related ultrasound abnormalities, perinatal outcome and association with assisted reproduction.

Keywords: Assisted reproductive technology; Conjoined twins; First trimester; Perinatal outcome; Prenatal diagnosis

Introduction

Conjoined twinning occurs in 1 in 100 sets of monozygotic twins, 1 in 50,000 gestations or 1 in 250,000 live births [1,2]. With the advent of ultrasound technology, prenatal diagnosis of conjoined twins is possible [3–5]. Fagan [6] first reported prenatal diagnosis of conjoined twins by ultrasonography at 32 weeks of gestation. Prenatal diagnosis of conjoined twins in the first trimester has also been well established following the introduction of transvaginal and high-resolution ultrasound. Schmidt et al. [7] first reported prenatal diagnosis of thoracoomphalopagus at 11 weeks of gestation. Since then, at least 75 cases (including two of ours) of conjoined twins detected in the first trimester (before 15 weeks of gestation) have been reported (Table 1).

Fetal gender, maternal age and parity

Table 1 shows that there is a female preponderance in conjoined twins. In this review, of 75 cases of conjoined twins, only 16 had sex determination by karyotyping or DNA study. The female: male ratio was 3:1 (12:4). In the first trimester, fetal genitalia cannot be diagnosed certainly, and cytogenetic or molecular investigation is required for sex determination. Machin and Keith [60] reported that about 75% of conjoined twins are female. This review also shows that in the first trimester, 75% (12/16) of conjoined twins are female. The average maternal age was 30.5 years ($n = 54$) (22–41 years). The parity ranged from P0 ($n = 28$), P1 ($n = 10$), P2 ($n = 10$)

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Table 1
Reported cases of conjoined twins diagnosed in the first trimester.

Authors	Maternal age (y)	Parity	ART	GS	Fetuses	GA at diagnosis (wk)	Classification	Sex	Ultrasound Abnormalities	Outcome
Present case 1 (Fig. 1)	38	P0	—	1	2	10	Ischiopagus	M	—	TOP
Present case 2 (Fig. 2)	35	P0	—	1	2	10	Thoracoomphalopagus	F	—	TOP
Mercan et al. [8]	32	P0	ICSI	1	2	10	Thoracopagus	NA	—	TOP
Osmanağaoğlu et al. [9]	31	P0	—	1	2	11	Thoracopagus	NA	—	TOP
Shim et al. [10]	30	P1	—	1	2	9	Thoracoomphalopagus	F	Anencephaly in one fetus	TOP
Varma et al. [11]	33	P0	IVF-ET	1	2	7	Thoracopagus	NA	—	IUFD at 9 weeks
Amin and Weekes [12]	25	P2	—	1	2	10	Thoracopagus	NA	Cystic hygroma	NA
DeStephano et al. [13]	37	P1	—	1	2	9	Omphalopagus	M	—	TOP
Poret et al. [14]	30	P0	ICSI	1	2	9	Thoracopagus	NA	—	TOP
Bornstein et al. [15]	41	P1	—	1	2	10	Thoracoomphalopagus	NA	—	TOP
Hirata et al. [16]	34	P1	ICSI	2	3	8	Thoracopagus	NA	—	IUFD of conjoined twins at 10 weeks. The other fetus was delivered smoothly at 39 weeks.
Taner et al. [17]	32	P0	—	1	2	7	Thoracopagus	F	—	IUFD at 7 weeks
Abu-Rustum and Adra [18]	26	P1	—	1	2	10	Thoracoomphalopagus	NA	—	IUFD
Mendilcioglu and Simsek [19]	22	P0	Clomiphene OI	3	4	11	Thoracopagus	NA	Increased NT	Selective feticide of the conjoined twins at 12 weeks. Other two fetuses were delivered smoothly at 36 weeks.
Ogutu et al. [20]	36	P0	—	1	2	11	Pygopagus	NA	—	Delivery at 35 weeks and successful separation at 2 months of age.
Allegra et al. [21]	38	P0	ICSI	3	4	11	Thoracoomphalopagus	F	Increased NT, edema	Selective feticide of the conjoined twins. Other fetus was delivered smoothly at 38 weeks.
Basgül et al. [22]	30	P0	—	1	2	9	Thoracoomphalopagus	F	Unilateral talipes in one fetus	TOP
Sherer et al. [23]	32	P3	—	1	2	7	Thoracopagus	NA	—	TOP
Schmid et al. [24]	30	P1	—	1	2	13	Cephalothoracopagus janiceps disymmetros	NA	Congenital heart defects	TOP
Suzumori et al. [25]	33	P2	—	2	3	13	Cephalothoracopagus janiceps disymmetros	F	—	TOP
Durin et al. [26]	39	P1	—	1	2	12	Cranio-rachi-pygopagus	NA	Right kidney agenesis	TOP
Fang et al. [27]	30	P1	—	1	2	9	Ischiopagus	NA	—	TOP
Maymon et al. [28]										
Case 1	33	P2	—	1	2	10	Thoracopagus	F	Increased NT, fetal hydrops	TOP
Case 2	37	P1	ICSI	3	4	11	Thoracopagus	NA	Increased NT	Selective feticide of the conjoined twins, embryo reduction to a single pregnancy. Other fetus was delivered smoothly at 38 weeks.
Pajkrt and Jauniaux [29]										
Case 3	NA	NA	—	1	2	11	Thoracopagus	NA	Increased NT	TOP
Case 4	NA	NA	—	1	2	8	Ischiopagus	NA	—	IUFD at 12 weeks
Case 5	NA	NA	—	1	2	12	Parapagus dicephalus tribrachius tetrapus	NA	Cystic hygroma, edema	IUFD at 14 weeks

(*continued on next page*)

Table 1 (*continued*)

Authors	Maternal age (y)	Parity	ART	GS	Fetuses	GA at diagnosis (wk)	Classification	Sex	Ultrasound Abnormalities	Outcome
Case 6	NA	NA	—	2	3	10	Parapagus dicephalus dibrachius dipus	NA	—	Selective feticide of the conjoined twins. Other fetus was delivered smoothly at term and alive.
Case 7	NA	NA	—	2	1	13	Parapagus dicephalus tribrachius dipus	NA	—	Delivery at 37 weeks. Unsuccessful separation with death of both twins.
Suzumori et al. [30]	28	P0	—	1	2	9	Parapagus dicephalus	NA	—	TOP
Vural and Vural [31]	24	P0	—	1	2	9	Parapagus	NA	—	IUFD at diagnosis
Daskalakis et al. [32]	29	P0	—	1	2	12	Pygopagus dicephalus tribrachius dipus	NA	—	TOP
Shimizu et al. [33]	36	P0	IVF-ET	1	2	10	Cephalopagus	F	—	TOP
Sepulveda et al. [34]										
Case 1	41	P2	—	2	3	13	Cephalopagus	NA	—	Selective feticide of the conjoined twins. Other fetus died *in utero* at 28 weeks.
Case 2	29	P2	—	2	3	10	Thoracopagus	NA	—	IUFD of the conjoined twins at 12 weeks. Other fetus was delivered smoothly at 38 weeks.
Sugawara et al. [35]	30	P0	ICSI	2	3	10	Thoracoomphalopagus	NA	—	IUFD of the conjoined twins. Other fetus was delivered smoothly at 38 weeks.
Mackenzie et al. [36]										
Case 1	NA	NA	—	1	2	14	Thoracoomphalopagus	F	—	Delivery at 34 weeks, alive. One twin died after separation, and one twin survived at age 14 months.
Case 8	NA	NA	—	1	2	14	Thoracoomphalopagus	M	—	TOP
Case 13	NA	NA	IVF-ET	1	2	9	Ischiopagus	F	—	IUFD at 17 weeks
Biswas et al. [37]	28	P0	—	1	2	13	Cephalothoracopagus janiceps monosymmetros	NA	—	TOP
Cuillier et al. [38]	NA	NA	—	1	2	13	Omphalopagus	M	—	TOP
Ohkuchi et al. [39]	23	P0	—	1	2	8	Thoracoomphalopagus	NA	—	TOP
Bega et al. [40]	29	P2	—	1	2	10	Craniopagus	NA	—	TOP
Goldberg et al. [41]	28	P0	ICSI	2	3	8	Thoracoomphalopagus	NA	—	Selective feticide of the conjoined twins. Other fetus was delivered smoothly at 37 weeks.
Kuroda et al. [42]	26	P0	—	1	2	13	Cephalopagus	NA	—	TOP
Lam et al. [43]	25	NA	—	1	2	10	Omphalopagus	NA	Hydrops in one co-twin	Selective reduction of the hydropic co-twin by thermocoagulation. The other co-twin was delivered smoothly at term.
Sebire et al. [44]										
Case 1	NA	NA	—	1	2	13	Thoracoomphalopagus	NA	—	TOP
Case 2	NA	NA	—	1	2	11	Thoracopagus	NA	—	TOP
Case 3	NA	NA	—	1	2	13	Thoracoomphalopagus	NA	—	TOP
Case 4	NA	NA	—	1	2	11	Thoracopagus	NA	—	TOP
Tongsong et al. [45]										
Case 1	20	P0	—	1	2	8	Parapagus diprosopus	NA	—	TOP
Case 2	30	P2	—	1	2	12	Thoracopagus	NA	—	TOP
Case 3	25	P0	—	1	2	11	Omphalopagus	NA	—	TOP

Bonilla-Musoles et al. [46]	24	P0	—	1	2	11	Thoracoomphalopagus	F	Increased NT in one twin and omphalocele in the other twin	TOP
Gardeil et al. [47]	34	P2	—	2	3	13	Thoracoomphalopagus	F	—	Delivery at 36 weeks. Neonatal death of the conjoined twins.
Lam et al. [48]										
Case 1	28	NA	—	1	2	8	Craniothoracopagus	NA	—	TOP
Case 2	30	P0	—	1	2	13	Thoracoomphalopagus	NA	—	TOP
Maymon et al. [49]	28	P1	—	1	2	10	Thoracoomphalopagus	NA	—	TOP
Van Eyndhoven and ter Brugge [50]										
Case 1	32	P1	—	1	2	12	Parapagus dicephalus dipus tetrabrachius	NA	Cystic hygroma in one fetus and omphalocele	TOP
Case 2	24	P0	—	1	2	11	Parapagus dicephalus dipus dibrachius	NA	—	TOP
Hill [51]	32	NA	ART	2	3	9	Ischiopagus	NA	Pentalogy of Cantrell of the conjoined twins	Selective feticide of the conjoined twins. IUFD of the normal triplet at 14 weeks.
Hubinont et al. [52]										
Case 1	NA	P2	—	1	2	11	Thoracoomphalopagus	NA	—	TOP
Case 2	NA	P0	—	1	2	9	Thoracoomphalopagus	NA	—	TOP
Levi et al. [53]	30	NA	—	NA	NA	10	NA	NA	—	TOP
Skupski et al. [54]	35	P2	IVF-ET	2	3	12	Thoracopagus	NA	—	Selective feticide of the conjoined twins. Other fetus was delivered smoothly at term.
Meizner et al. [55]	NA	NA	—	1	2	9	Thoracoomphalopagus	NA	—	TOP
Boulot et al. [56]	27	P0	IVF-ET	2	3	10	Craniopagus	NA	—	Selective feticide of the conjoined twins. Other fetus was delivered smoothly at term.
Fontanarosa et al. [57]	30	P1	—	1	2	11	Parapagus diprosopus	NA	Craniorachischisis and left gastroschisis	TOP
Barth et al. [58]										
Case 2	NA	NA	—	1	2	11	Thoracoomphalopagus	NA	Bilateral lymphangiectasia	TOP
Case 3	NA	NA	—	1	2	12	Thoracoomphalopagus	NA	Small omphalocele	TOP
Case 6	NA	NA	—	1	2	14	Thoracopagus	NA	Congenital heart defects	Delivery at 38 weeks. Neonatal death of the conjoined twins.
Case 8	NA	NA	—	1	2	9	Parapagus diprosopus	NA	—	TOP
Case 10	NA	NA	—	1	2	13	Omphalopagus	NA	Omphalocele	TOP
Maggio et al. [59]	35	P3	—	1	2	13	Thoracoomphalopagus	NA	—	TOP
Schmidt et al. [7]	23	P0	—	1	2	11	Thoracoomphalopagus	NA	—	TOP

ART = assisted reproductive technology; F = female; GS = gestational sac; GA = gestational age; ICSI = intracytoplasmic sperm injection; IUFD = intrauterine fetal death; IVF-ET = *in vitro* fertilization and embryo transfer; M = male; NA = not available; — = no; OI = ovulation induction.

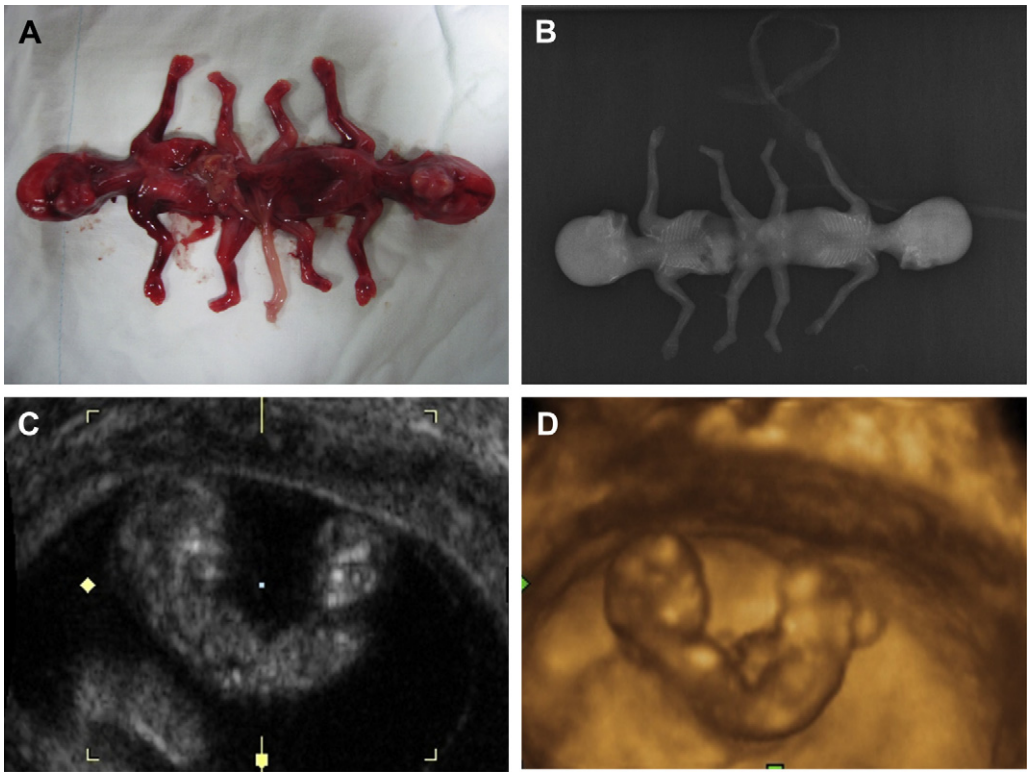

Fig. 1. Case 1. (A) A case of ischiopagus delivered at 12 weeks of gestation. (B) Radiograph of ischiopagus. (C) Two-dimensional (2D) ultrasound of ischiopagus at 10 weeks of gestation. (D) 3D ultrasound of ischiopagus at 10 weeks of gestation.

to P3 ($n = 2$). There is no association with maternal age and parity in the cases with conjoined twins.

Types of fusion

The reported types of fusion among 74 cases of conjoined twins with known types of fusion in this review include thoracoomphalopagus ($n = 24$), thoracopagus ($n = 18$), parapagus ($n = 10$), cephalothoracopagus ($n = 4$), ischiopagus ($n = 5$), omphalopagus ($n = 5$), craniopagus ($n = 2$), cephalopagus ($n = 3$), pygopagus ($n = 2$) and cranio-rachi-pygopagus ($n = 1$). Ventral unions such as rostral, caudal and lateral unions occur most commonly (69/74 = 93.2%). Cephalopagus including cephalothoracopagus occurs in 9.5% (7/74). Thoracopagus occurs in 25.7% (19/74). Omphalopagus including thoracoomphalopagus occurs in 37.8% (28/74). Ventral rostral unions such as thoracopagus, omphalopagus and cephalopagus occur most commonly (54/74 = 73%). Ventral lateral union such as parapagus occurs in 13.5% (10/74). Ventral caudal union such as ischiopagus occurs in 6.8% (5/74). Dorsal unions such as craniopagus, rachipagus and pygopagus occur less commonly (5/74 = 6.8%). Spencer [61] suggested that eight types of pagus (Greek term as fixed or joined) conjoined twins should be recognized such as omphalopagus (umbilicus), thoracopagus (chest), cephalopagus (head), ischiopagus (hip), craniopagus (helmet), rachipagus (spine), pygopagus (rump) and parapagus (side). Other additional terms include the numerals di- (two), tri- (three) and tetra- (four), and the united anatomical structures such as prosopus (face), brachius (upper limb) and pus (lower limb). Spencer [62] also suggested that conjoined twins should be classified by the proposed site of union and be divided into two groups of ventral (joined over a single yolk sac with a shared abdomen and umbilicus) including those united rostrally, caudally and laterally; and dorsal (joined in the neural tube with a separate abdomen and umbilical cord in each twin). The ventral rostral group includes cephalopagus (top of head to umbilicus), thoracopagus (thorax, upper abdomen and conjoined heart) and omphalopagus (thorax, upper abdomen and separate hearts). The ventral caudal group includes ischiopagus (lower abdomen and genitourinary tract). The ventral lateral group includes parapagus (pelvis and variable trunk) including diprosopus (2 faces) and dicephalus (2 heads). The dorsal group includes craniopagus (cranial vault), rachipagus (vertebral column) and pygopagus (sacrum). In a study of 1200 actual cases of conjoined twins, Spencer [62] found that ventral group accounts for 87% including rostral (48%) (cephalopagus: 11%, thoracopagus: 19%, omphalopagus: 18%), caudal (11%) and lateral (28%), and that dorsal group accounts for 13% including craniopagus (5%), rachipagus (2%) and pygopagus (6%). Cephalothoracopagus janiceps refers to conjoined twins with fused thorax and fused head which has two faces each looking in opposite directions [3,5]. The term janiceps is derived from Janus, a two-faced Roman god. When the two faces are identical and symmetrical, it is called janiceps disymmetros, whereas when the two faces are dissimilar with only one complete face and the other reduced face showing varying degrees of differences in the completeness of a face, it is called janiceps monosymmetros [63,64].

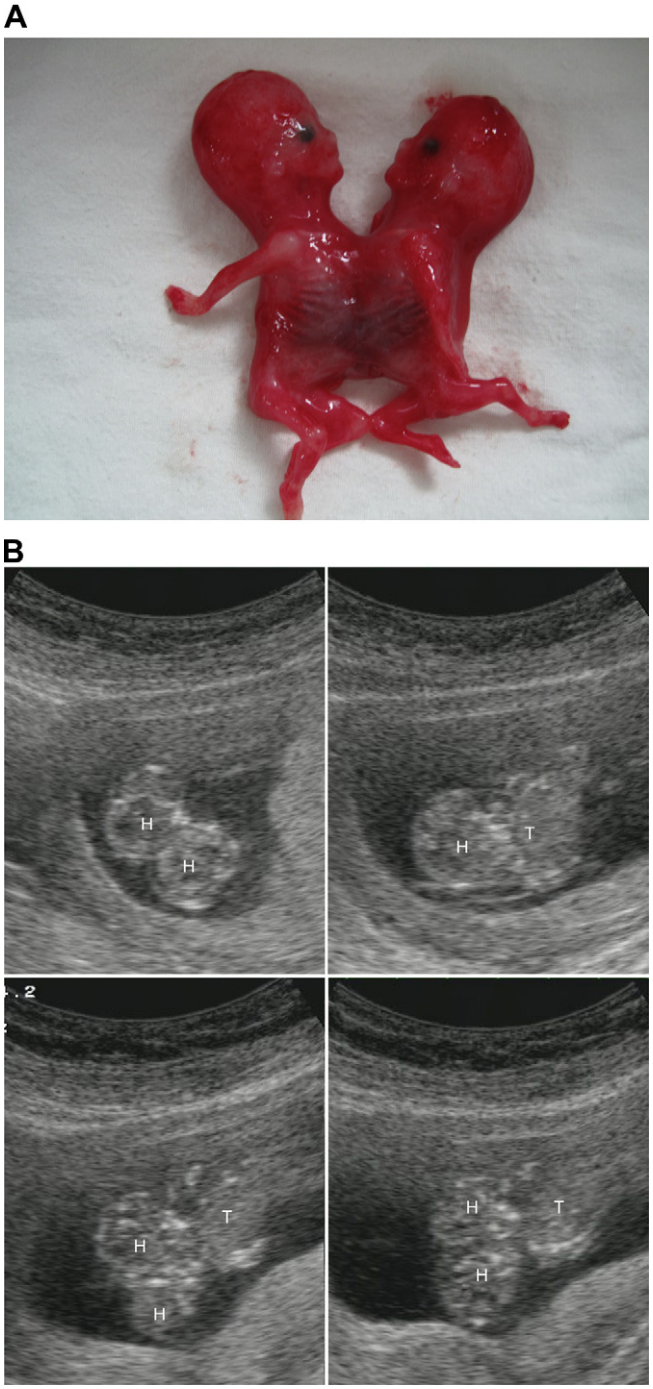

Fig. 2. Case 2. (A) A case of thoracoomphalopagus delivered at 11 weeks of gestation. (B) Two-dimensional (2D) ultrasound of thoracoomphalopagus at 10 weeks of gestation. H = head, T = thorax.

Related ultrasound abnormalities

Table 1 shows that ultrasound abnormalities were found in 19 (25.3%) of 75 conjoined twins detected in the first trimester. The abnormalities include increased nuchal translucency (NT) ($n = 6$) (6/75 = 8%), lymphangiectasia ($n = 1$) (1/75 = 1.3%), hydrops fetalis and edema, ($n = 4$) (4/75 = 5.3%), cystic hygroma ($n = 3$) (3/75 = 4%), abdominal wall defects (omphalocele, gastroschisis or pentalogy of Cantrell) ($n = 6$), neural tube defects (anencephaly and craniorachischisis) ($n = 2$), congenital heart defects ($n = 2$), talipes ($n = 1$) and renal agenesis ($n = 1$). Lymphedema ($n = 11$) (11/75 = 14.7%) such as lymphangiectasia, hydrops, edema, cystic hygroma and/or increased NT is the most common related anomaly associated with conjoined twins detected in the first trimester. Sebire et al. [44] found increased NT in six co-twins of four set conjoined twins. Hemodynamic disturbance due to abnormalities of the heart and great arteries and disturbed or delayed lymphatic development may be in part associated with increased NT in conjoined twins [19,44,65]. In this review, all cases associated with increased NT are cases of thoracopagus or thoracoomphalopagus. Since thoracopagus conjoined twins have extensively shared hearts, it is likely that the shared cardiovascular system and the abnormalities of the heart cause cardiac insufficiency and subsequent increased NT and subcutaneous edema which may be detected in the first trimester [28]. In this review, conjoined twins can be associated with birth defects linked to the conjoining such as omphalocele in omphalopagus, or birth defects not obviously linked to the conjoined such as neural tube defects and congenital heart defects. In a study of 81 sets of conjoined twins, Edmonds and Layde [1] reported the most common congenital malformations not obviously associated with the fusion were neural tube defects ($n = 6$), orofacial clefts ($n = 6$), imperforate anus ($n = 6$), diaphragmatic hernia ($n = 6$), congenital heart defects ($n = 6$), cryptorchidism ($n = 3$) and ambiguous genitalia ($n = 3$).

Perinatal outcome

Out of 75 cases of conjoined twins detected in the first trimester, 60 (80%) were terminated or received feticide, eight (10.7%) had intrauterine fetal death, and only six (8%) were carried to term, indicating half of the conjoined twins who have escaped termination or fetal reduction will suffer from intrauterine fetal death. Of the six sets of conjoined twins carried to term, only four twins of three sets of conjoined twins survived. The first case was pygopagus reported by Ogutu et al. [20]. The twins were delivered at 35 weeks and had successful separation at 2 months of age. The second case was thoracoomphalopagus reported by Machenzie et al. [36]. The twins were delivered at 34 weeks and had demise of one twin after separation but survival of the other twin at age 14 months. The third case was omphalopagus reported by Lam et al. [43]. The twins had received *in utero* selective reduction of the hydropic twin by thermocoagulation, and the other twin was delivered at term and survived.

Association with assisted reproduction

Of the 75 cases of conjoined twins, 14 (18.7%) had undergone assisted reproductive technologies (ART) such as *in vitro* fertilization and embryo transfer (IVF-ET) ($n = 5$), intracytoplasmic sperm injection (ICSI) ($n = 7$), ovulation induction ($n = 1$) and others ($n = 1$). In this review, about 80% of the conjoined twins with assisted reproduction were

reported within the past decade, indicating the risk of conjoined twins should be kept in mind in all ART cycles at the present time. Monozygotic twinning (MZT) has been reported to occur at a significantly higher rate following ART compared with the natural incidence [66]. Various hypotheses have been raised as the etiology of MZT such as ovulation induction [67]; assisted hatching [68], blastocyst transfer [69,70], ICSI [70,71], culture conditions [72], embryologist's experience [73] and blastocyst culture [74]. In a systemic review and meta-analysis of the risk of MZT after ART, Vitthala et al. [75] found the summary incidence of MZT after ART was 0.9%, indicating a risk of MZT in ART being 2.25 times higher than the incidence of 0.4% in natural conception. They also found the calculated MZT rates for different ARTs were 1.2% for ovulation induction, 0.35% for IVF, 0.97% for ICSI, 3.0% for frozen ET, 1.7% for blastocyst transfer and 0.7% for assisted hatching. They suggested that ICSI and blastocyst transfer carry higher risk of MZT than conventional IVF or assisted hatching, and ICSI and blastocyst transfer are associated with 2.25 and 4.25 times higher risk of MZT, respectively.

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