WHAT IS THE SURVIVAL RATE IN PRENATALLY DETECTED CANTRELL'S PENTALOGY?

Authors:
Katarzyna Pośpiech-Gąsior[1], Maciej Słodki[2,3], Maria Respondek-Liberska[2,4]

1.Perinatology Clinic of the Collegium Medicum, Jagiellonian University, Krakow 2. Department of Prenatal Cardiology, Polish Mother's Memorial Hospital Research Institute, Lodz, Poland, 3. Institute of Health Sciences, The State School of Higher Professional Education in Płock, Poland 4. Medical University of Lodz, Department of Diagnoses and Prevention Fetal Malformations

Prenat Cardio 2016 Jan; 6(1):31-36
DOI: 10.1515/pcard-2016-0004

Abstract

Cantrell's pentalogy is a congenital defect characterized by uncompleted fusion of the anterior chest wall, resulting in an extrathoracic location of the heart. Ultrasound diagnosis during the first trimester of prenatal life is possible, and termination of pregnancy is usually chosen by pregnant women. We analysed 57 fetuses: 56 from literature and one additional recent case from our institute (from 2016) to evaluate what was the survival rate reported after prenatal diagnosis, including the possibility to terminate the pregnancy, intrauterine deaths and neonatal deaths. We found 10 survivors - 18% since 1984.

Despite dismal prognosis of fetal ectopia cordis, there is a chance for postnatal survivorship probably due to evolving anatomical structures, not only in the first trimester of pregnancy but also during the following weeks of prenatal life.

Key words: *ectopia cordis, Cantrell syndrome, diaphragmatic hernia*

INTRODUCTION

Cantrell's pentalogy is an anomaly resulting from a defect in embryologic development and consists of the following: a deficiency of the anterior diaphragm, a midline supra-umbilical abdominal wall defect, a defect in the diaphragmatic pericardium, congenital intracardiac abnormalities and a defect of the lower sternum.

MATERIAL AND METHODS

We analyzed the published reports of prenatal Cantrell's pentalogy from the literature, since 1984, which were detected in 1st or second trimester of pregnancy. (Table 1), and focused on the gestational age at the time of diagnoses, number of termination of pregnancies, intrauterine demises and neonatal follow-up.

How to cite this article:
Pośpiech-Gąsior K, Słodki M, Respondek-Liberska M. What is the survival rate in prenatally detected Cantrell's pentalogy ? Prenat Cardio 2016; 6(1):31-36

The last case from 2016 from our institution is presented below:

A 28-year-old woman (G1, P0) had no history of intake of any teratogens or exposure to unusual environment during the antenatal period. The family history was negative for congenital anomalies or genetic abnormalities, and there was no-cosanguinity. A screening ultrasound at 12 weeks of pregnancy revealed a nuchal translucency of 3,8 mm, nasal bone present and omphalocele (containing liver, stomach and cardiac apex)(Foto 1, 2-cine, 3). Biochemical tests of maternal blood showed PAPPA-A of 0,3 MoM and free bHCG of 0,733 MoM. Chorionic villus sampling was nondiagnostic and amniocentesis showed a karyotype of 46, XX. The pregnant women was offered termination of pregnancy, however, she decided to continue her pregnancy and to deliver at a tertiary obstetrical and cardiac center. Prenatal echocardiography at 18, 20, 27 and 30th week of gestational age revealed a four-chamber heart with normal flow in the great arteries. Ultrasound biometry was adequate. At 27 th week due to visualization of intestines in fetal chest cavity suggesting diaphragmatic hernia (DH), MRI examination was offered and right anterior DH was confirmed. In the second half of pregnancy, the position of the fetal heart and size of omphalocele changed: there was an improvement in 'niche' in the fetal chest and a decrease in size of the fetal omphalocele. At 38th week of gestation, an elective Cesarean section was performed, and a baby girl, with birth weight of 2,800g, and Apgar score of 8/8, was delivered. Physical examination confirmed an exposed heart outside of the thoracic cavity without pericardium. The abdominal wall defect caused evisceration of liver, stomach and intestines. Neonatal echocardiography showed mild functional mitral and tricuspid regurgitation

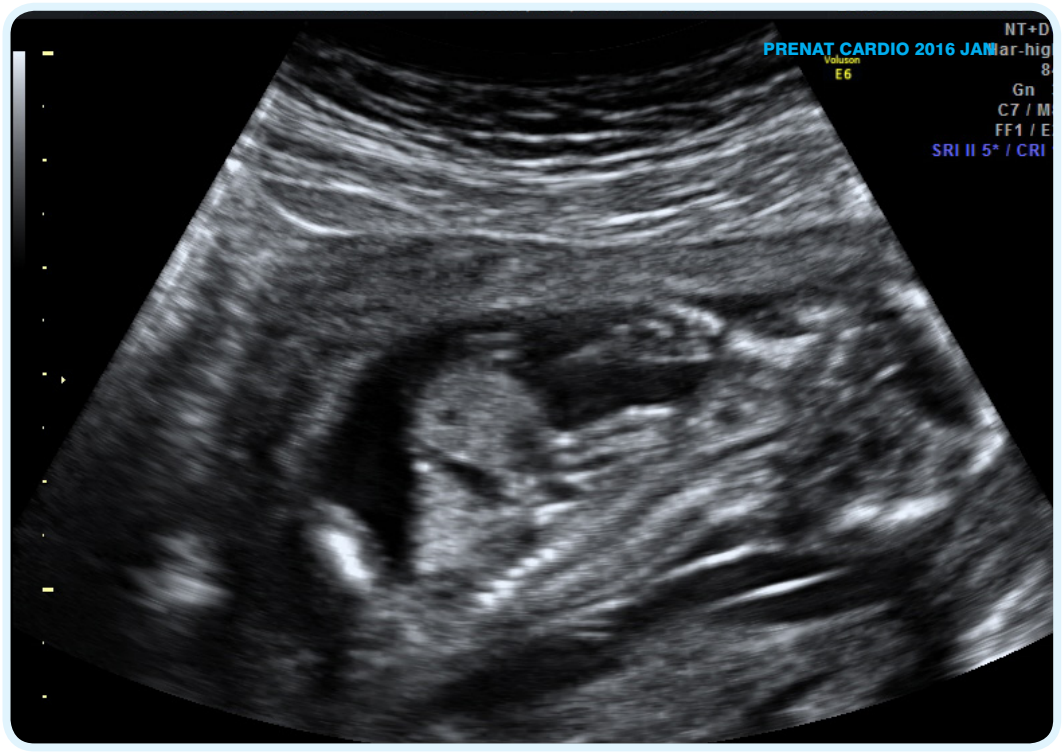
Corresponding author: majkares@uni.lodz.pl

Submitted: 2015-12-11, accepted: 2016-01-18

Year of Publication	Authors	Gestational age of the detection of EC	Nr of fetuses	Termination of pregnancy	In utero demise	Death after delivery	Survivors
1984	Haynor DR, Shuman WP, Brewer DK, Mack LA. [8]	II trim.	4	0	1	3	0
1991	Achiron R, Shimmel M, Farber B, Glase [9]	18 weeks	1	0	0	1	0
1995	Dillon E, Renwick M.[10]	I trim.	3	1	0	0	2
1998	Hsieh YY, Lee CC, Chang CC, Tsai HD, Hsu TY, Tsai CH.[11]	I trim.	2	2			
1999	Bognoni V, Quartuccio A, Quartuccio A.[12]	11 weeks	2	2	0	0	0
1999	Tongsong T, Wanapirak C, Sirivatanapa P, Wongtrangan S.[13]	9 weeks, 13, 21, and 29 weeks	4	2	0	1	1
2000	Repondek-Liberska M, Janiak K, Wloch A.[14]	Average 26 weeks	7		4	3	0
2000	Colpaert C, Bogers J, Hertveldt K, Loquet P, Dumon J, Willems P.[15]	I trim.	1	1			0
2002	Mittermayer C, Bernaschek G, Lee A.[16]	12,4	1	1			0
2003	Smrcek JM, Gembruch U, Krokowski M, Berg C, Krapp M, Geipel A, Germer U.[17]	11,1; 11, 1; 12; 13, 1 wks	4	4			0
2003	Onderoğlu L, Baykal C, Tulunay G, Talim B, Kale G.[18]	12 wks	1	1			0
2005	Staboulidou I, Wüstemann M, Schmidt P, Günter HH, Scharf A.[19]	10 wks	1	1			0
2006	Gomez S, Bermlúez Sosa MT, Palma Hernández E, del Castillo Salceda LF, Pinzón Muslera O, Hernández Cortés B, Méndez Machado G.[20]	27 wks	1	0			1
2008	Ziddere i Allan [21]		3				3
2009	Peixoto-Filho FM, do Cima LC, Nakamura-Pereira M.[22]	10 wks 11 wks	2	1	1 1		0
2009	Barbee K, Wax JR, Pinette MG, Cartin A, Blackstone J.[23]	I trim. - Twin	1	1			Selective fetal reduction of EC fetus, delivered a healthy 3065g female infant
2010	Hannoun A, Usta IM[31], Sawaya F, Nassar AH.[24]	10 wks	1	1			1
2011	Sadłecki P, Krekora M, Krasomski G, Walentowicz-Sadłecka M, Grabiec M, Moll J, Respondek-Liberska M. [25]	15 wks	1				1
2013	Di Spiezio Sardo A, Paladini D, Zizolfi B, Spinelli M, Nappi C.[26]	I, early II trim.	2	2			
2013	Sepulveda W, Wong AE, Simonetti L, Gomez E, Dezerega V, Gutierrez J.[27]	I trim. - 7 fetuses with EC	7	2	2	2	1 died at 3 months of age.
2014	Y S, K T, M I, S S.[28]	I trim. – 4 fetuses with EC	4	3	1		0
2015	Türkçapar AF, Sargın Oruc A, Öksüzoglu A, Danışman N.[29]	12 wks	1	1			0
2015	Pekin AT, Kerimoğlu OS, Yilmaz SA, Kebapcilar AG, Bakbak BG, Celik C.[7]	12 wks	1	1			0
2016	Pośpiech-Gąsior K, Respondek-Liberska M.	13 wks	1	0	0	0	1
Total number of ectopia cordis in fetuses in years 1984 until today*			**57**	**27**	**10**	**10**	**10**

* 7 follow-up presumly dead

Table 1. Ectopia cordis (EC)- literature review: prenatal diagnoses of ectopia cordis < 30 weeks of gestation.



Fot. 1 2D presentation: Fetus at 12th week of gestation with omphalocele including fetal heart

and X-ray confirmed right diaphragmatic hernia (Fot. 4). The single-stage closure of the abdominal defect and reposition of the ectopic heart was performed without any complications. (Fot. 5).

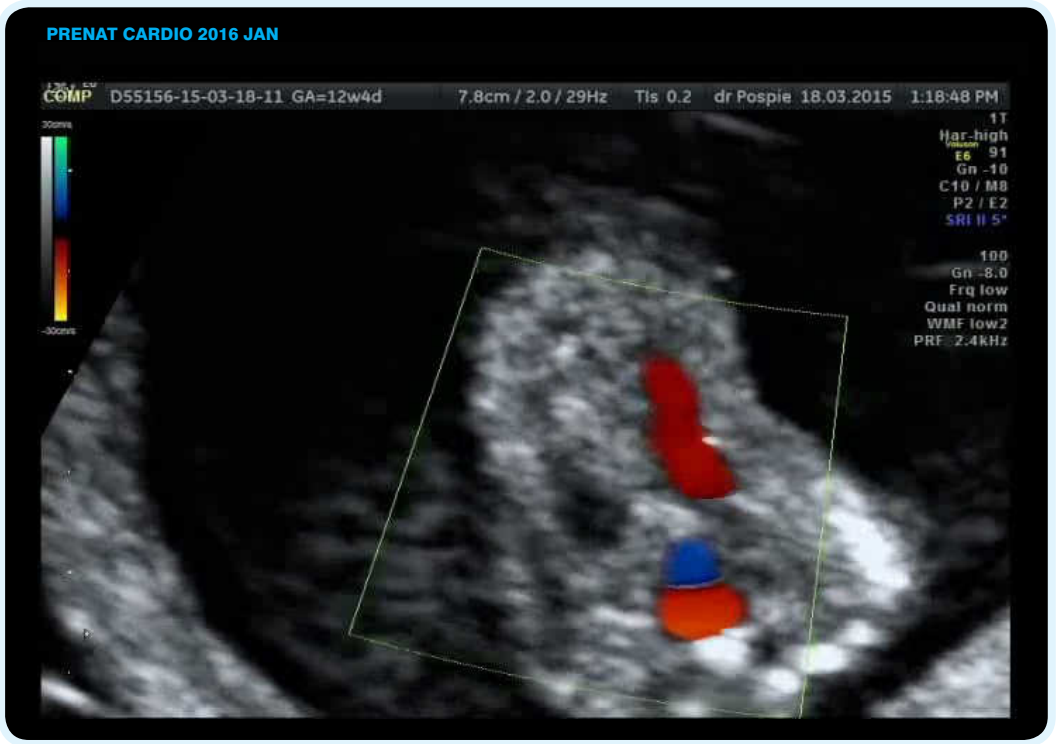
As shown in table 1 , first trimester detection of ectopa cordis is common, and it was reported in almost 50% of cases. In 46% (27 cases) there was decision about termination of pregnancy. In 18% (10 cases) there was spontaneous intrauterine demise later on. In 8 cases there was lost follow-up.

Finally we found 9 survivors – 16%, including the most recent case presented above (as a second one from our Institution)[25].

DISCUSSION

First described in 1958, Cantrell's pentalogy is a syndrome of congenital defects characterized by lack of fusion of the anterior chest wall, resulting in an extrathoracic location of the heart[1]. It is more common among males and comprises 0.1% of congenital heart diseases, with a prevalence of 1/65,000–1/200,000 live births. Ectopia cordis can be classified into cervical, thoracic, thoraco-abdominal or abdominal types, according to the location of the heart. Ectopia cordis may occur as an isolated malformation or may be associated with body wall defects that affect the thorax, abdomen or both. This malformation of the heart can occur with normal heart anatomy or heart defect, usually ToF, DORV, d-TGA, VSD, CAT and others[2,3,4].

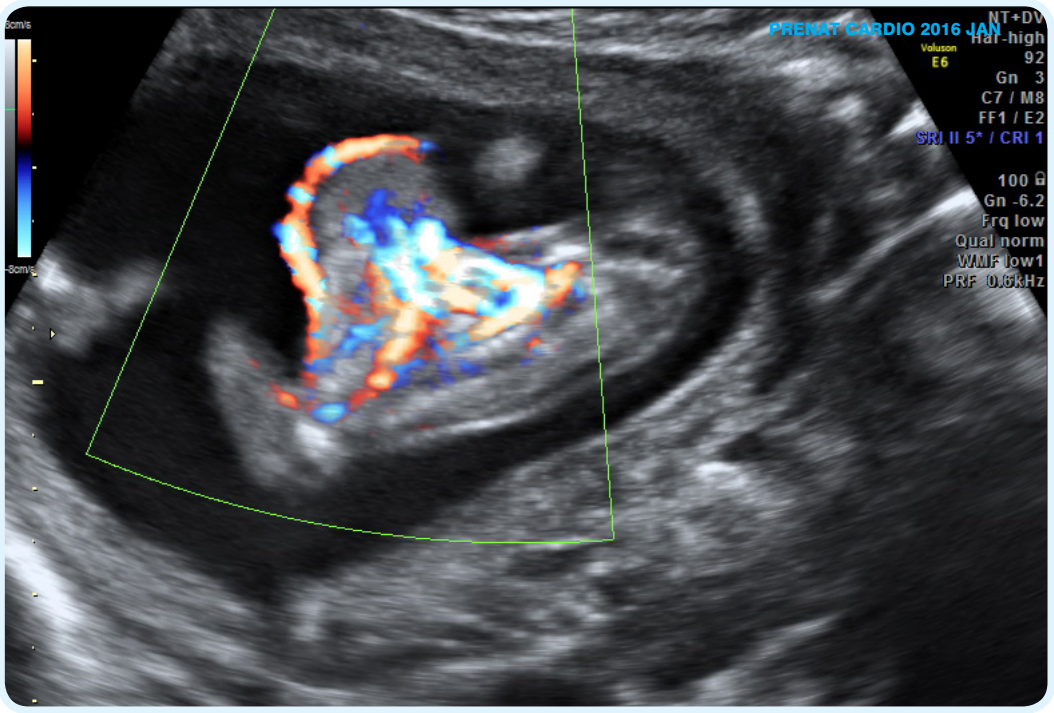
The pathogenesis of Cantrell's pentalogy is unclear, and the syndrome is considered of heterogeneous origin. Cantrell and co-workers postulated a developmental failure in differentiation of a segment of the lateral mesoderm around the 14–18th day of embryonic life. Consequently, the transverse septum of the diaphragm does not



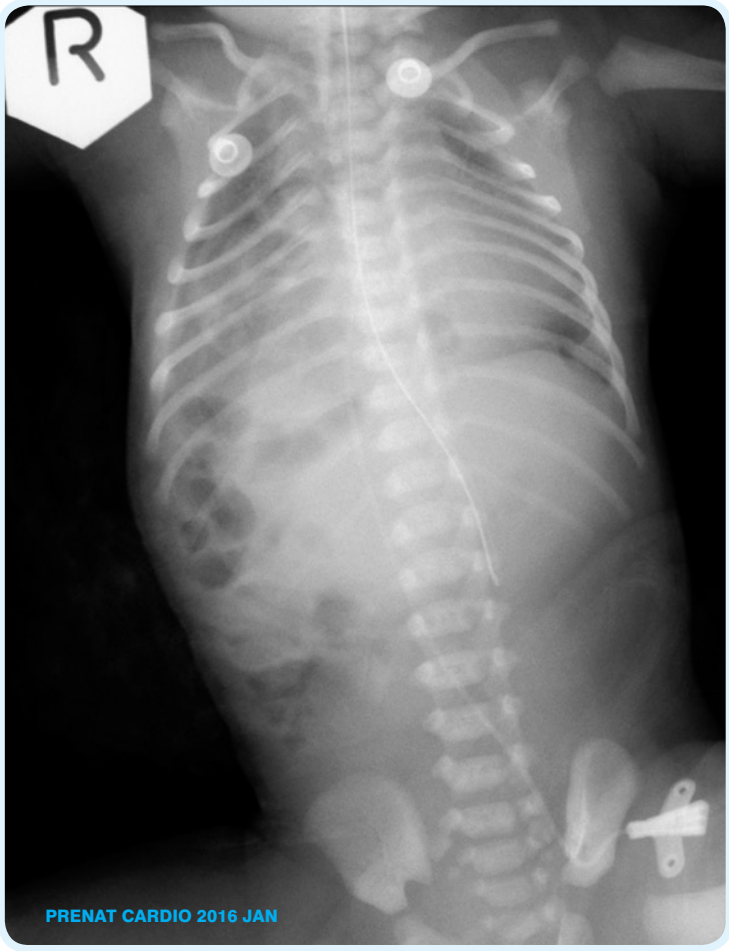
Fot. 2 (cine): In 2DD cine presentation with color Doppler the fetal heart outised of the fetal thorax at 12th week of pregnancy

Play the movie directly in the pdf by clicking on the content

develop and the paired mesodermal folds of the upper abdomen do not migrate ventromedially. Organs may thus eviscerate through the resulting sternal and abdominal wall defects. Mechanical teratogens were suggested, however, most cases are sporadic and the etiology is still unknown[5]. Only a few patients display the full spectrum of anomalies.



Fot 3: Fetus at 12th week of gestation with power Doppler technique



Fot 4: Neonatal chest X-ray just after delivery showing right diaphragmatic hernia

In 1972, Toyama[6] proposed additional classification of the syndrome: class I, confirmed diagnosis with all five defects present; class II, probable diagnosis with four defects noted (including intracardiac and ventral abdominal wall abnormalities); and class III, incomplete expression with various combinations of defects, always including sternal anomalies. Regardless, in "pure" Cantrell's syndrome or Cantrell's pentalogy with other anomalies, the prognosis is always poor and perinatal mortality is high[4,5,7].

Diagnosis of Cantrell's pentalogy with modern ultrasonography during prenatal life is possible during the first trimester, as early as even the 9th week of gestation (Table 1)[7-31]. The differential diagnosis includes isolated thoracic ectopia cordis, amniotic band syndrome, and body stalk anomaly (Table 2). The key features in distinguishing these conditions is the position of abdominal wall defect in relation to the umbilical cord insertion, eviscerated organs, presence or absence of membranes or bands and associated anomalies. Omphalocele in Cantrell's pentalogy usually involves a midline defect at the umbilical cord insertion. The ectopic heart may either simply bulge out of the chest or be entirely out of the chest.

Associated diaphragmatic hernia could make the prognosis even worse. Therefore, to have a better prenatal assessment, magnetic resonance imaging (MRI) is applied in addition to ultrasonography. As suggested by Donofrio[30], ectopia cordis currently belongs to those fetal cardiac abnormalities for which a specialized delivery room should be an option with a multi-specialist perinatal team (consisting of an obstetrician, neonatologist, prenatal cardiologist, anaesthestologist, pediatric surgeon, special midwife and nurses).

As shown in Table 1, in the published literature, 10 (17%) of 57 fetuses with ectopia cordis diagnosed

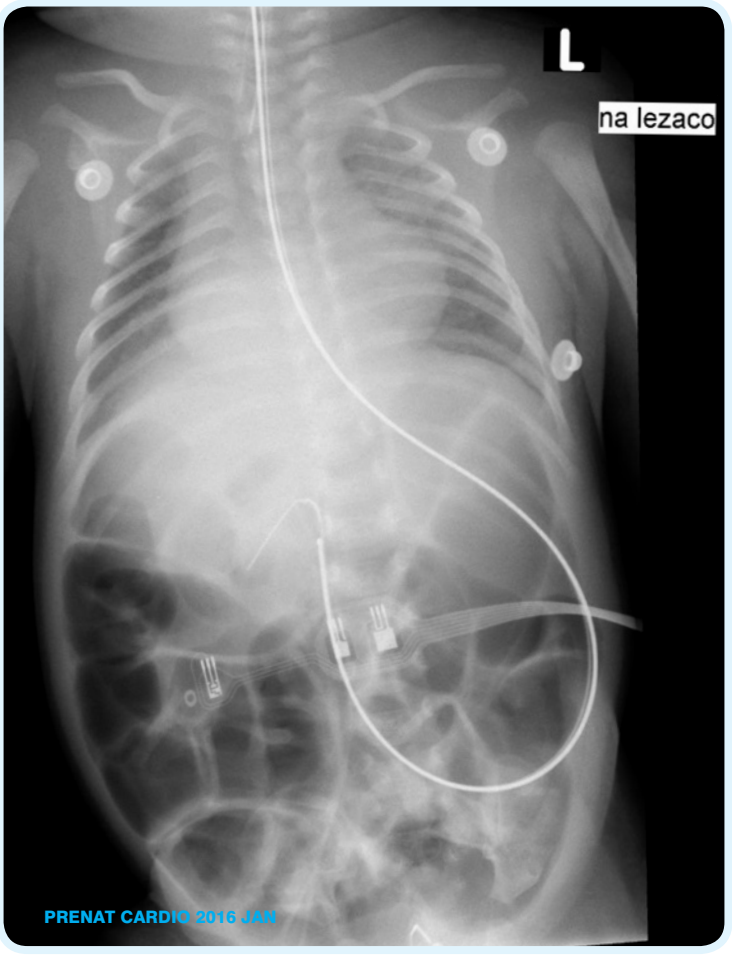
Pentalogy of Cantrell	Sternal, pericardial and diaphragmatic defects, omphalocele
Beckwith-Wiedemann syndrome	Organomegaly, polyhydramnios, macroglossia, large omphalocele
Amniotic band syndrome	Random defects, constriction rings, amputations, bands
Limb-body wall complex	Complex-looking mass entangled with membrane, limb anomalies, spinal anomalies

Table 2. Ectopia cordis – differential diagnosis.

before 30 weeks of gestation survived: two presented by Dillon in 1995[10], one by Tongsong and co-workers in 1999[13] , one in Spain reported in 2006[20], three cases in U.K in 2008[21], one presented by Węgrzynowski and co-workers[31] and two cases from our institution. The first case[25] was discharged at the 4th week of postnatal life, but died suddenly 10 months later. The other, presented above, had an extremely difficult postnatal management period, but ended successfully and we do believe its postnatal surgery and intensive care treatment deserves a separate presentation.

CONCLUSIONS

Despite the dismal prognosis of fetal ectopia cordis and ectopia cordis diagnosed early in pregnancy, the postnatal survivorship is as high as 18%, probably due to evolving anatomical structures not only in first trimester of pregnancy but also during the following weeks of prenatal life.



Fot 5: Neonatal chest X-ray just after delivery showing right diaphragmatic hernia

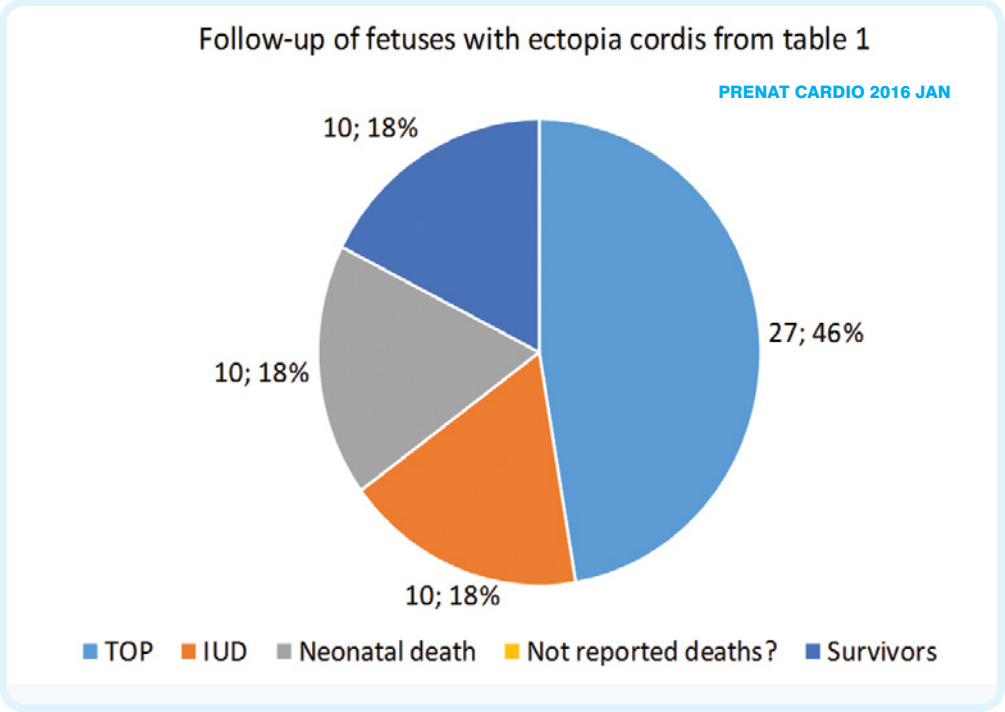


Fig. 1. Follow-up of fetuses with ectopia cordis from table 1

ACKNOWLEDGEMENTS

We would like to thank our colleagues who took care of our patients in medical centers in Kraków and Łódź: Dr. B. Radzymińska-Chruściel (Ujastek, Kraków), Dr. A. Pięta-Dolińska (ICZMP, Łódź), Prof. I. Moroszyńska and her team from the Neonatal Intensive Therapy and Congenital Malformations Department (ICZMP, Łódź), Prof. A. Piaseczna-Piotrowska and her team from the Pediatric Surgery Department (ICZMP, Łódź), Prof. P. Grzelak, from the Radiology Department (ICZMP, Łódź), Prof. M. Stasiołek from the Pediatric Neurology Department (ICZMP, Łódź), Prof. J. Moll from Pediatric Cardiac Surgery Department (ICZMP, Łódź) and Dr. M. Machnia from the Rehabilitation Department (ICZMP, Łódź).

Nr of survivors	Authors	%	Country
3 /57 2/57	Zidere V, Allan LD. Dillon E, Renwick M.	5% 3%	UK, London North England
1.03.1957	1.Sadłecki P, Krekora M, Krasomski G, Walentowicz-Sadłecka M, Grabiec M, Moll J, Respondek-Liberska M, 2.Rajewska J, Gawrych E, Węgrzynowski J, Konefał H, Rybkiewicz M. 3. Katarzyna Pośpiech-Gąsior , Maciej Słodki, Maria Respondek-Liberska.	5,00%	Poland
1.01.1957	Tongsong T, Wanapirak C, Sirivatanapa P, Wongtrangan S.	2,00%	Thailand
1.01.1957	Gomez SG, Bermulez Sosa MT, Palma Hernandez E, del Castillo Salceda LF, Pinzon Muslera O, Hernandez Cortes B, Mendez Machado G.	2,00%	Spain

Table 3. Survivors after prenatal diagnosis of ectopia cordis in relation to the country

References

1. Cantrell JR, Haller JA, Ravitch MM. A syndrome of congenital defects involving the abdominal wall, sternum, diaphragm, pericardium, and heart. Surg Gynecol Obstet. 1958;107:602–614.

2. Desselle C, Herve P, Toutain A, Lardy H, Sembely C, Perrotin F. Pentalogy of Cantrell: sonographic assessment. J Clin Ultrasound. 2007;35:216–220.

3. Khoury MJ, Cordero JF, Rasmussen S. Ectopia cordis, midline defects and chromosome abnormalities: an epidemiologic perspective. Am J Med Genet. 1988;30:811–817.

4. Respondek-Liberska M, Janiak K, Kaczmarek P, Borowski D, Czichos E. The significance of cardiography in the diagnosis of cardiac ectopia of the fetus. Ginekol Pol. 1998;69:139-144. Polish.

5. Kaplan LC, Matsouka R, Gilbert EF, Opitz JM, Kurnit DM. Ectopia cordis and cleft sternum: evidence for mechanical teratogenesis following rupture of the chorion or yolk sac. Am J Med Genet. 1985;21:187–202.

6. Toyama WM. Combined congenital defects of the anterior abdominal wall, sternum, diaphragm, pericardium, and heart: a case report and review of the syndrome. Pediatrics 1972;50:778–786.

7. Pekin AT, Kerimoğlu OS, Yilmaz SA, Kebapcilar AG, Bakbak BG, Celik C. Pentalogy of Cantrell accompanied by scoliosis and pes equinovarus deformity at 12 weeks gestation. Clin Exp Obstet Gynecol. 2015;42:392–394.

8. Haynor DR, Shuman WP, Brewer DK, Mack LA. Imaging of fetal ectopia cordis: roles of sonography and computed tomography. J Ultrasound Med. 1984;3:25–27.

9. Achiron R, Shimmel M, Farber B, Glaser J. Prenatal sonographic diagnosis and perinatal management of ectopia cordis. Ultrasound Obstet Gynecol. 1991;1:431–434.

10. Dillon E, Renwick M. The antenatal diagnosis and management of abdominal wall defects: the northern region experience. Clin Radiol. 1995;50:855–859.

11. Hsieh YY, Lee CC, Chang CC, Tsai HD, Hsu TY, Tsai CH. Prenatal sonographic diagnosis of Cantrell's pentalogy with cystic hygroma in the first trimester. J Clin Ultrasound. 1998;26:409-412.

12. Bognoni V, Quartuccio A, Quartuccio A. First-trimester sonographic diagnosis of Cantrell's pentalogy with exencephaly. J Clin Ultrasound. 1999;27:276–278.

13. Tongsong T, Wanapirak C, Sirivatanapa P, Wongtrangan S. Prenatal sonographic diagnosis of EC. J Clin Ultrasound. 1999;27:440–445.

14. Respondek-Liberska M, Janiak K, Wloch A. Fetal echocardiography in ectopia cordis. Pediatr Cardiol. 2000;21:249-252.

15. Colpaert C, Bogers J, Hertveldt K, Loquet P, Dumon J, Willems P. Limb-body wall complex: 4 cases illustrating the importance of examining placenta and umbilical cord. Pathol Res Pract. 2000;196:783–790.

16. Mittermayer C, Bernaschek G, Lee A. Diagnosis of ectopia cordis with three-dimensional power Doppler ultrasound in first-trimester pregnancy. Ultrasound Obstet Gynecol. 2002;20:203–205.

17. Smrcek JM, Gembruch U, Krokowski M, Berg C, Krapp M, Geipel A, Germer U. The evaluation of cardiac biometry in major cardiac defects detected in early pregnancy. Arch Gynecol Obstet. 2003;268:94-101.

18. Onderoğlu L, Baykal C, Tulunay G, Talim B, Kale G. Prenatal diagnosis of Cantrell's pentalogy: a case report. Turk J Pediatr. 2003;45:357–358.

19. Staboulidou I, Wüstemann M, Schmidt P, Günter HH, Scharf A. Increased fetal nuchal translucency as a predictor of Cantrell's pentalogy - case report. Z Geburtshilfe Neonatol. 2005;209:231-234.

20. Gomez SG, Bermulez Sosa MT, Palma Hernandez E, del Castillo Salceda LF, Pinzon Muslera O, Hernandez Cortes B, Mendez Machado G. Ectopia cordis: multidisciplinary approach with successful result. Ginecol Obstet Mex. 2006;74:439–443.

21. Zidere V, Allan LD. Changing findings in pentalogy of Cantrell in fetal life. Ultrasound Obstet Gynecol. 2008;32:835–837.

22. Peixoto-Filho FM, do Cima LC, Nakamura-Pereira M. Prenatal diagnosis of Pentalogy of Cantrell in the first trimester: is 3-dimensional sonography needed? J Clin Ultrasound. 2009;37:112-114.

23. Barbee K, Wax JR, Pinette MG, Cartin A, Blackstone J. First-trimester prenatal sonographic diagnosis of ectopia cordis in a twin gestation. J Clin Ultrasound. 2009;37:539–540.

24. Hannoun A, Usta IM, Sawaya F, Nassar AH. First trimester sonographic diagnosis of ectopia cordis: a case report and review of the literature. J Matern Fetal Neonatal Med. 2011;24:867–869.

25. Sadłecki P, Krekora M, Krasomski G, Walentowicz-Sadłecka M, Grabiec M, Moll J, Respondek-Liberska M. Prenatally evolving ectopia cordis with successful surgical treatment. Fetal Diagn Ther. 2011;30:70–72.

26. Di Spiezio Sardo A, Paladini D, Zizolfi B, Spinelli M, Nappi C. Pentalogy of Cantrell: embryofetoscopic diagnosis. J Minim Invasive Gynecol. 2013;20:248–251.

27. Sepulveda W, Wong AE, Simonetti L, Gomez E, Dezerega V, Gutierrez J. Ectopia cordis in a first-trimester sonographic screening program for aneuploidy. J Ultrasound Med. 2013;32:865–871.

28. Shibata Y, Terada K, Igarashi M, Suzuki S. Body stalk anomaly complicated by ectopia cordis in the first trimester. J Clin Diagn Res. 2014;8:OD06-7.

29. Türkçapar AF, Sargin Oruc A, Öksüzoglu A, Danışman N. Diagnosis of pentalogy of cantrell in the first trimester using transvaginal sonography and color Doppler. Case Rep Obstet Gynecol. 2015;2015:179298.

30. Donofrio MT, Levy RJ, Schuette JJ, Skurow-Todd K, Sten MB, Stallings C, Pike JI, Krishnan A, Ratnayaka K, Sinha P, du Plessis AJ, Downing DS, Fries MI, Berger JT. Specialized delivery room planning for fetuses with critical congenital heart disease. Am J Cardiol. 2013;111:737–747.

31. Rajewska J, Gawrych E, Wegrzynowski J, Konefał H, Rybkiewicz M. Cantrell's pentalogy - a case report. Ginekol Pol. 2010 Nov; 81(11): 860-4.

Division of work:

M. Respondek-Liberska – concept of this manuscript and final version

M. Słodki - work with manuscript

K. Katarzyna Pośpiech-Gąsior – detection of malformation, introduction of the record to the Polish National Registry of Fetal Cardiac Malformations, author of prenatal ultrasound pictures, first draft, and literaturę search

Conflict of interest: The authors declare no conflict of interest

Authors do not report any financial or personal links with other persons or organizations, which might affect negatively the content of this publication and/or claim authorship rights to this publication