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Perinatal Autopsy Evaluation of 2150 Autopsies in the Çukurova Region of Turkey

Çukurova Bölgesinden 2150 Perinatal Otopsi Olgusunun Değerlendirilmesi

Arbil AÇIKALIN[1], Emine KILIÇ BAĞIR[1], Goncagül TORUN[1], Berna TOTAN ATEŞ[1], Şeyda ERDOĞAN[1], Aysun UĞUZ[1], Melek ERGİN[1], Selim BÜYÜKKURT[2], Fatma TUNCAY ÖZGÜNEN[2], Nurdan TUNALI[1], Derya GÜMÜRDÜLÜ[1]

Departments of [1]Pathology and [2]Obstetrics and Gynecology, Çukurova University, Faculty of Medicine, ADANA, TURKEY

ABSTRACT

Objective: We aimed to document the reasons of perinatal deaths in a large autopsy series performed in our institute, which is a reference center in the Çukurova region of Turkey.

Material and Method: The study included 2150 autopsies performed between January 2000 and December 2012at our institute. Diagnoses were categorized according to the detected pathologies; congenital malformations were detailed based on systems.

Results: A pathology was detected in 1619 of 2150 (73.3%) autopsies. Congenital malformations were the most common diagnosis with 68.2%. Neural tube defects and central nervous system malformations were the most frequent system malformation in 28.8% of cases, followed by the urogenital system (11.4%) and musculoskeletal system (8.3%), respectively. Malformation syndromes including multisystem anomalies were defined in 109 cases (9.3%).

Conclusion: Congenital malformations are the most common reason for perinatal deaths, with autopsy having an additive role to prenatal and genetic evaluations and providing foresight for planning a subsequent pregnancy.

Key Words: Autopsy, Congenital abnormalities, Prenatal diagnosis, Perinatal mortality, Syndrome

ÖZ

Amaç: Türkiye'nin Çukurova bölgesi için referans merkez konumunda olan ve oldukça geniş otopsi serisi içeren kurumumuzda yapılan fetal otopsi olgularını, değerlendirerek perinal ölüm nedenlerini tespit etmeyi amaçladık.

Gereç ve Yöntem: Ocak 2000 ve Aralık 2012 yılları arasında kurumumuza gelen 2150 adet otopsi raporu yeniden değerlendirildi. Olgular tanılarına göre gruplandırıldı. Ayrıca konjenital malformasyonlar yer aldıkları sistemlere göre alt gruplara ayrıldı.

Bulgular: Toplam 2150 olgunun 1619'unda (%73,3) patolojik bulgu saptandı. En sık patoloji %68,2 oranında konjenital malformasyonlar idi. Nöral tüp defektleri ve santral sinir sistemi anomalileri en sık malformasyon idi (%28,8). Bunu sırasıyla ürogenital sistem (%11,4) ve kas-iskelet sistemi (%8,3) takip etmekteydi. Bunun yanısıra, 109 olguda (%9,3) çoklu sistem tutulumu gösteren malformasyon sendromları tanımlandı.

Sonuç: Fetal otopsi prosedürü, son yıllarda sayısal düşüş göstermekle birlikte, özellikle gebelik beklentisi olan kişiler için, prenatal tarama yöntemlerine tanısal katkısı olmakta ve malformasyonun yineleme olasılığı hakkında öngörü sağlamaktadır.

Anahtar Sözcükler: Otopsi, Doğumsal anomaliler, Prenatal tanı, Perinatal mortalite, Sendrom

INTRODUCTION

The stillbirth rate of a population is accepted as an indicator of development. This factor has an impact on evaluating the reasons of prenatal and postnatal deaths to decrease the stillbirth rates. In a large pooled analysis, Lawn et al. have estimated that 26% (1.02 million) of the total number of 3.9 million stillbirths are intra-partum stillbirths (1). Congenital malformations are frequent reasons of intrauterine death, and the distribution of the incidence of abnormalities differs by region. It is important to identify the distribution and prevalence of congenital abnormalities for every country and even every region (2). Çukurova University is a reference center for pregnancies at risk in the Çukurova region of Turkey. This region shows a higher incidence of consanguineous marriages, lower social and cultural levels, and particular environmental factors that possibly increase perinatal mortality rates. We perform approximately 200 ± 50 autopsies per year at our institute. In present study, we aimed to present a large series including 2150 autopsy results within a 13-year period, and to document the distribution of the causes of perinatal death in the Çukurova region.

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Correspondence: Arbil AÇIKALIN
Çukurova Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı,
01130, Sarıçam, ADANA, TURKEY
E-mail: arbilavci@yahoo.com Phone: +90 532 470 21 20

MATERIAL and METHODS

This retrospective study includes 2150 prenatal and postnatal (under one year-old) autopsies performed at our institute between January 2000 and December 2012 (13 years). The autopsy technique and expectations from autopsy were described to the family member of the fetus by the obstetrician and/or pathologist (in case of the family's request) and a consent form was obtained. The option of receiving the fetus after the autopsy procedure is provided to the family members because of religious reasons. After the consent, all cases were X-rayed from the anterior and lateral aspects. Photographs were taken at all stages of the procedure, especially in terms of the presence of abnormalities. Circumferences of the head, chest and abdomen; head to heel, head to sacrum, and heel to second toe lengths; and weight of the fetus and the visceral organs were measured and noted. The fetus was incised using the "Y" method, and the visceral organs were taken out as three separate compartments (thorax, abdomen, genitourinary), dissected and sampled. We excluded 437 stillbirths where gross and microscopic evaluation results were not eligible due to severe autolysis. The findings of the 1713 other cases were categorized according to the congenital malformations, placental factors, infections and miscellaneous diagnoses.

Congenital malformations were sub-categorized according to isolated system abnormalities, multi-system abnormalities and chromosomal defects. We also analyzed and compared the distribution of the number of cases by the 13 years.

RESULTS

Distribution of autopsy numbers per year is shown in Figure 1. The male to female ratio was 1044/1039. The gender could not be detected in 65 fetuses because of severe autolysis and maceration, and 2 cases had ambiguous genitalia. The most frequent fetal age was the second trimester as found in 1388 cases (64.5%), followed by the third trimester in 627 (29.2%) cases and first trimester in 79 cases (3.7%). Thirty-nine cases (1.8%) were newborn (0-1 month) and 17 (0.8%) were infants (1-12 months). Newborns and infants were more common in the years 2000-2005 years while second trimester infants were more common after 2006. Ninety-four cases (4.3%) were normal with no gross, microscopic or genetic pathologies. The most frequent diagnosis was congenital abnormalities as found in 1169 cases (68.2%). Chorioamnionitis associated with early membrane rupture, categorized in placental factors, was the second most common diagnosis and found in 228 cases (10.6%). Other pathologies are listed with their frequencies in Table I.

Table I: Distribution of the diagnoses of 1713 autopsies

Congenital malformations	1169 (68.2%)
Placental factors	277 (16.2%)
No pathologic findings	94 (5.5%)
Intracranial hemorrhage	56 (3.3%)
Meconium aspiration	52 (3.1%)
Intrauterine growth retardation and related problems	33 (1.9%)
Infection	18 (1.0%)
Twin-twin transfusion	14 (0.8%)
Total	**1713 (100%)**

Frequencies of single system congenital abnormalities other than syndromes and chromosomal defects were as follows from highest to lowest: neural tube defects and central nervous system anomalies (Figure 2); nuchal edema / cystic hygroma; urogenital system; skeletal system; cardiovascular system; abdomen wall and diaphragm defects; and respiratory system pathologies. Abnormalities with respect to systems are listed in Table II.

Chromosomal defects were detected in 48 cases (2.2%) and were as follows: 15 trisomy 21 cases, 13 trisomy 13 cases, 2 Turner syndrome (45, X0) cases, 2 Klinefelter syndrome (47, XXY) cases and 3 others (18p deletion, aneuploidy and digynic triploidy).

Multisystem abnormalities including defined syndromes are listed in Table III (Figure 3,4). Live births (39 newborns, 17 infants) showed mostly infections, problems associated with prematurity, and metabolic/storage diseases. Infections were present in 6 cases of which 3 were CMV, 2 Parvovirus and 1 Toxoplasmosis. A congenital tumor was detected in five cases and all were teratomas (Figure 5).

DISCUSSION

Congenital malformations are one of the most common causes of perinatal deaths and our rate was 68.2%. Fetal autopsy is accepted to be as important as and perhaps even more important than karyotype analysis and prenatal ultrasonography in comparative studies in the literature (3-7). Fetal autopsy provided more information than prenatal ultrasonography in these studies. Any information is important for the obstetrician who has to answer the questions of families about the risk of recurrence in following pregnancies. Our results showed a marked decrease in annual autopsy numbers from 270 to 170s, especially in last 2 years (Figure 1). There are many reasons for this, such as: detailed information about the benefits of fetal autopsy is not provided to family members in contrast to past years due to the heavy workload and social security problems. Fetal autopsy leads

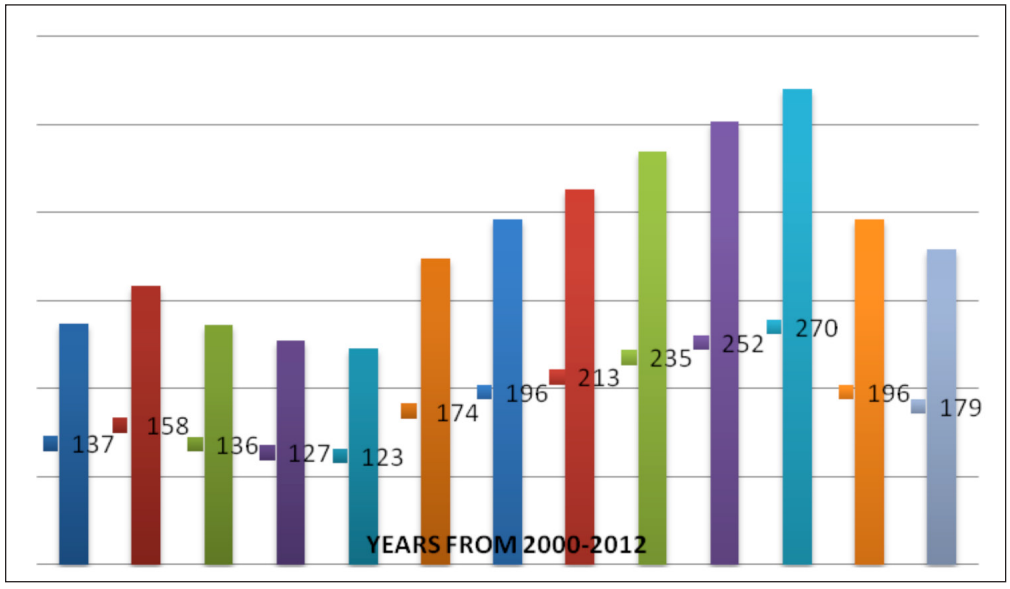

Figure 1: Number of autopsies performed in our institute from 2000 to 2012 per year.

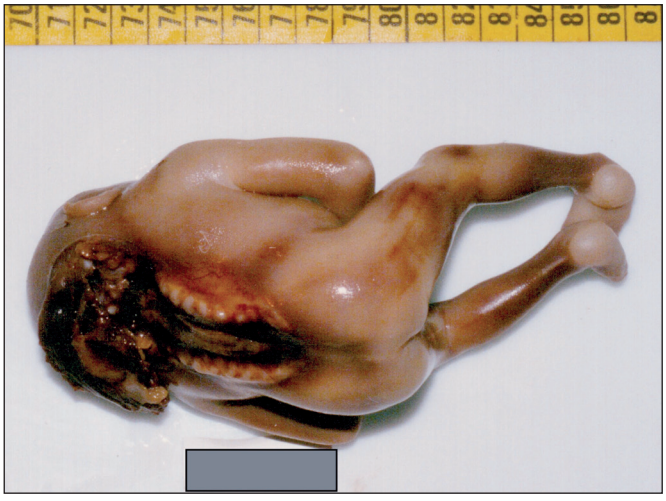

Figure 2: Fetus with neural tube defect showing anencephaly and iniencephaly.

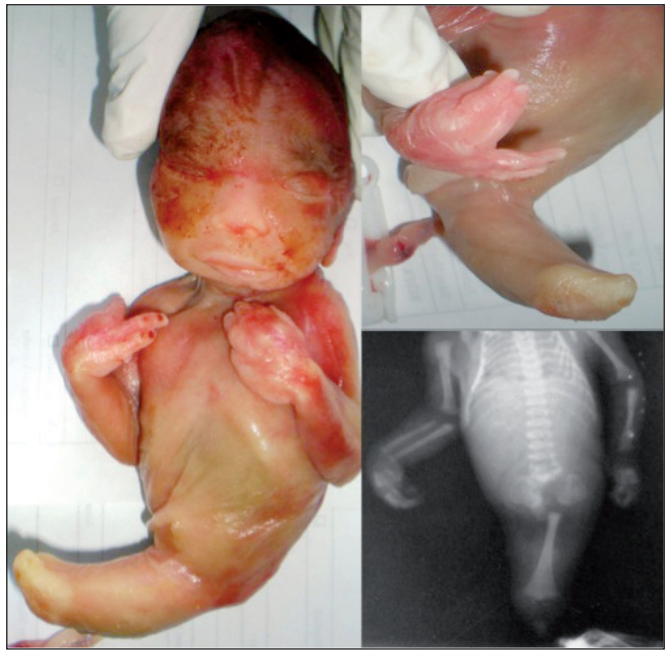

Figure 3: Gross and X-ray findings of a fetus with syrenomelia/ mermaid syndrome.

to extra cost and is not paid by social security. Social security does not pay for fetal autopsy consultations requested from other institutions. All these factors collectively have a negative effect on the number of autopsies performed.

Causes of perinatal and postnatal deaths were detected and/ or supported by fetal autopsy in 1619 of 2150 (75.3%) cases in the present study. The most frequent reason of death was congenital malformations (68.2%) in our study, due to the fact that most of our group was in the second trimester, i.e. the anatomical scanning period. Neural tube defects and central nervous system abnormalities were the most common abnormality in 337/1169 cases (28.8%) in our study and this was similar to the rate of 31.1-74.2% reported in the literature (2, 6-8). The vast majority of this group consisted of spina bifida (meningocele / meningomyelocele), seen in 121 cases, followed almost equally by anencephaly in 118 cases. NTD cases are consistently reported at high rates in the literature as they are easily detected on prenatal ultrasonography (2).

The second most frequent abnormality in previous studies was either musculoskeletal system or urogenital system abnormalities as we also observed (7, 9, 10). Most of the

Table II: Distribution of congenital malformations based on systems

Diagnoses	n (%)
Neural tube defects/CNS malformations	**337 (28.8%)**
Spina bifida (meningocele/ meningomyelocele) Anencephaly	121
Ventriculomegaly ±	118
Hydrocephalus	50
Encephalocele	20
Holoprocencephaly	12
Corpus callosum defect	4
Dandy-Walker malformation	4
Arnold-Chiari malformation	3
Iniencephaly	5
Urogenital system malformations	**133 (11.4%)**
Multicystic renal dysplasia	56
Renal agenesis	41
Obstructive uropathy	17
Horseshoe kidney	12
Infantile polycystic renal disease	4
Renal tubular dysgenesis	1
Ambiguous genitale	2
Musculoskeletal system malformations	**97 (8.3%)**
Osteochondrodysplasia	49
Poly-/Syn-/Brachy-dactily	47
Mitochondrial DNA defect	1
Cardiovascular system malformations	**88 (7.5%)**
Atrial septal defect	21
Ventricular septal defect	19
Atrial and ventricular septal defects	5
Truncus arteriosus	6
Fallot tetralogy	3
Hypoplastic left heart	1
Dextrocardia	2
Patent ductus arteriosus	2
Pulmonary artery stenosis	2
Complex abnormalities	27

Diagnoses	n (%)
Gastrointestinal system/Abdominal wall/ Diaphragm malformations	**85 (7.3%)**
Gastroschisis	32
Omphalocele	29
Diaphragm hernia	8
Malrotation	3
Meckel diverticule	6
Ectopia/Heteropia	7
Respiratory system malformations	**34 (2.9%)**
Hyalen membrane disease	13
Pulmonary hypoplasia	11
Cystic adenomatoid malformation	6
Bronchopulmonary dysplasia	1
Ekstra/Intrapulmonary sequestration	3
Chromosomal defects	**48 (4.1%)**
Trisomy 21	15
Trisomy 13	13
Trisomy 18	13
Turner (45, XO)	2
Klinefelter (47, XXY)	2
Dygynic triploidy	1
Aneuploidy	1
18 p deletion	1
Miscellaneous	
Teratoma	5
Cleft lip/palate	37
Hydrops fetalis with unknown etiology	136
Nuchal edema	59
Chronic granulomatous disease of childhood	1

cases were multicystic dysplasia (56/133) and renal agenesis (41/133). Renal abnormalities are usually associated with severe oligohydramnios and are therefore easy to detect in the prenatal period.

Half of the 97 musculoskeletal system anomalies consisted of osteochondrodysplasia with 49 cases. These abnormalities were evaluated by the obstetrician as a skeletal anomaly. Postmortem X-ray radiographies were evaluated by a radiologist and additive findings of microscopic evaluation of the bones enabled us to subcategorize the dysplasia in majority of cases.

Cardiovascular system anomalies are not easy to detect in the early weeks and in stillborn fetuses as the vascular structures are very fine and sensitive to dissection. Septal defects were the most frequent anomalies (45 of 88 cases) followed by complex anomalies in 27 cases, similar to the results of Ramalho et al. (11).

Isolated system anomalies of solid organs and vertebra are usually detected during prenatal ultrasonography. Fetal autopsy has an additive role, particularly in complex anomalies and defined syndromes found at a rate of 109/1169 in our study. These complex anomalies may be

Figure 4: Neu-Laxova syndrome.

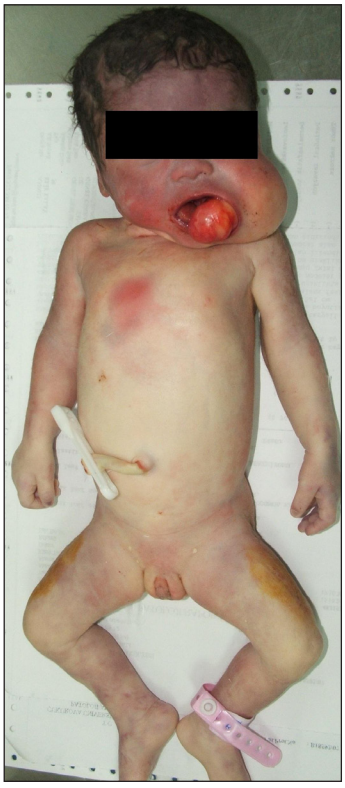

Figure 5: Fetus with intraoral teratoma.

Table III: Diagnosis of defined congenital malformation syndromes

Diagnoses	n
Meckel-Gruber syndrome	19
Potter sequence	17
Limb-Body-Wall defect	9
Lethal multiple ptergium syndrome	7
Syrenomelia/Mermaid syndrome	8
Neu-Laxova Syndrome	4
Prune-Belly syndrome	3
VACTERL syndrome	3
Body Stalk anomaly	3
Situs Inversus Totalis	3
Fraser syndrome	3
Amniotic band syndrome	4
Metabolic / storage diseases	7
Acardiac fetus	3
TRAP syndrome	1
Robert's syndrome	2
Beckwith wiedeman syndrome	1
Leigh syndrome	1
Cloacal dysgenesis	1
Penoshokeir Phenotype 1	1
Cornelia de Lange syndrome	1
Oro-facio-digital syndrome	1
Baller Gerold syndrome	1
Jarcho Levin syndrome	1
Harlequin fetus	1
Fetus papyraceus	1
Trachophagus	1
Craniophagus	1
VATER associaton	1
Total	**109**

genetically inherited, or may have a high recurrence risk and therefore need to be defined to guide genetic evaluations. We have detected a wide range of congenital malformation syndromes as listed in Table III.

The aim of this study was to focus on congenital malformations but it is of note that there was a high incidence of autolysis related to undetected intrauterine deaths with 20.3% (437/2150) of the cases, where the autopsy procedure could not detect an abnormality even if present. The benefits of autopsy need to be evaluated in this aspect so that the request can be selective to avoid overloading the health care and social security systems.

To summarize, this large series of 13 years of results showed that congenital malformations are the most common reason of perinatal deaths, and autopsy has an important role that is additional to genetic evaluation to predict the risk of recurrence in the following pregnancies.

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