

# Retrospective analysis of pregnancy terminations and indications in a tertiary center

Sureyya Saridas Demir<sup>1,\*</sup>, Erkan Çağliyan<sup>1</sup>, Sabahattin Altunyurt<sup>1</sup>

<sup>1</sup> Department of Obstetrics and Gynecology, Division of Perinatology, Dokuz Eylul University School of Medicine, 35340 Izmir, Turkey

\*Correspondence: [drsurreyyademir@hotmail.com](mailto:drsurreyyademir@hotmail.com) (Sureyya Saridas Demir)

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**Purpose:** The aim of this study was to evaluate the indications of pregnancies terminated which were for maternal and fetal causes in our clinic and to discuss legal and ethical issues differing by countries. **Methods:** This study was performed retrospectively by evaluating 318 pregnancies terminated due to maternal or fetal indications over 10 weeks. **Results:** Termination of pregnancy was performed due to fetal congenital, chromosomal and obstetrical reasons in 96.8% of 318 terminated cases and due to maternal reasons in 3.2% of them. Thirty-two (10%) late termination cases with gestational week  $> 23 + 0$  were termed after feticide procedure. **Conclusion:** Gestational limit for termination of pregnancy varies from country to country, which brings ethical problems with it. We presented indications of pregnancy terminations in our clinic, which is a tertiary and reference center within the legal framework.

## Keywords

Chromosomal and fetal abnormalities; Prenatal diagnosis; Termination of pregnancy

## 1. Introduction

Major congenital abnormalities are among the leading causes of infant mortality [1]. The most common causes of perinatal mortality are antepartum stillbirths (42.7%), problems associated with prematurity (26.0%) and fatal congenital malformations [2]. Soft markers in the genetic sonogram and chromosomal abnormalities in the presence of major congenital anomalies is a very useful diagnostic modality of ultrasonography in determining fetuses [3].

International fetal abnormality screening programs play an important role in the early diagnosis of congenital abnormalities. The optimal time to perform the combined test [nuchal translucency (NT), pregnancy-associated plasma protein A (PAPP-A) and free beta-human chorionic gonadotrophin (beta-hCG)] is between  $11^{+2}$  and  $14^{+1}$  weeks of gestation according to the National Health Service (NHS) Fetal Abnormality Screening Program (FASP) [4]. USG is recommended at the second trimester to screen fetal abnormalities for all pregnancies between  $18^{+0}$ - $20^{+6}$  gestational weeks. The objectives of the screening programs are; to determine the conditions that can be benefit from the treatment before or after the delivery, to optimize the delivery of the birth in an appropriate hospital or center, to optimize the

treatment of the baby after the birth and to identify the abnormalities that will end in death shortly after the delivery [4].

Fetal structural and chromosomal abnormalities which detected in early gestational weeks and any abnormalities caused a risk for mother life could be regarded as the main indications for termination of pregnancy (TOP) [5]. Gestational age is the most important parameter for the termination decision of pregnancy for fetal abnormality (TDPA) [6]. The diagnosis of fetal abnormality is an unexpected serious emotional trauma for the mother and the family. Women may face various difficulties, even if she accepts the continuation of pregnancy or elective termination [7].

There is not yet an international standard for pregnancy evacuations that should be performed due to medical indications. On the other hand yet, there is no accepted guideline regarding termination indications made for medical reasons. For now, legal regulations of every country determine the principles of TOP according to range of gestational weeks and maternal, fetal and other specific criminal-cultural indications. In this study, we aimed to evaluate the termination indications of pregnancies performed in our clinic that is a tertiary center and to discuss legal and ethical issues differing by countries.

## 2. Materials and methods

The present study focuses on 318 pregnant women admitted to Dokuz Eylul University School of Medicine, Department of Obstetrics and Gynecology, Division of Perinatology between 1 January 2015 and 31 December 2018 for termination of their pregnancies evaluated retrospectively. Among these dates, 148 of the 5342 births that took place in our clinic were death births. Of the 318 pregnancies that were terminated, 245 were due to fetal congenital anomalies. Pregnancies terminated due to maternal or fetal indications over 10 weeks by decision of the perinatology council were included and pregnancies that were less than 10 weeks and terminated voluntarily were excluded. Various countries have various regulations for TOP. In some countries, TOP after 10 weeks is strictly prohibited by the law. According to the laws where the study took place, termination of pregnan-

cies over 10 weeks is considered to be a crime. Again, due to the fact that our study is on fetuses with anomalies, pregnancies that have been terminated without a medical reason were not included in this study. The socio-demographic characteristics of women whose pregnancy were terminated with medical indication were recorded in the anamnesis form. The socio-demographic features, age, gestational weeks, parity, fetal weight, termination indications were demonstrated in Table 1. Fetal USG examinations were performed by Voluson P6 GE Medical Systems device in perinatology outpatient clinic by the same physician. Fetal magnetic resonance imaging (MRI) was performed as an additional imaging method to confirm the diagnosis (especially for central nervous system and chest abnormalities) in indicated pregnancies.

**Table 1. Demographic and clinical characteristics of pregnant women.**

n = 318	Mean	Minimum	Maximum
Age	31.38 ± 6.30	18	46
Gravida	2.22 ± 1.34	1	7
Parity	0.80 ± 0.85	0	5
Gestational week	18.20 ± 3.67	11	30
Fetal weight (gr)	215.76 ± 137.8	50	900

TOP indications were divided into two main groups; fetal (congenital, chromosomal, obstetric) and maternal causes. Fetal causes were central nervous system abnormalities (CNS), chromosomal disorders, preterm premature rupture of membranes (PPROM), multiple fetal abnormalities, cardiovascular abnormalities, oligo-anhydramnios, genitourinary system abnormalities, musculoskeletal abnormalities, cystic hygroma, hydrops fetalis and chest abnormalities (Table 2,3). Maternal causes were due to hypertensive diseases in pregnancy, maternal systemic diseases and conditions, cardiovascular diseases and teratogen drug use (Table 2). All indications were evaluated and approved by the perinatology council ethics committee consisting by at least three consultant; newborn specialist, pediatric cardiology, neurology, radio-diagnostics, surgery, medical genetics and/or pharmacology specialists. All pregnant women included in the study were healthy and had no additional diseases (preeclampsia, diabetes, anemia, cholestasis, etc.). Additionally, no woman had a newborn with an anomaly before. Or therefore pregnancy termination has not occurred.

Misoprostol was used as the first choice for the evacuation of fetuses over the 10th gestational week. Misoprostol protocol was administered orally, sublingually or vaginally according to the gestational week and the history of the pregnant woman in accordance with clinical guidelines protocols [10, 11]. Induction with oxytocin was performed in cases whose gestational termination with misoprostol did not occur within 48-72 hours. In the uterine cavity control after fetal abortion, manual or electronic vacuum aspiration curettage was used to clean the placenta or its residues.

This study was conducted in accordance with the principles of the Helsinki Declaration and Institutional Ethical Committee approved this study (Approval number: 5152-GOA; 2019/31-13; the date of issue: 16.12.2019).

The results were calculated using SPSS Statistics 20 software. The data were reported as the mean ± standard deviation (minimum-maximum) and the percentage.

### 3. Results

The women whose pregnancy was terminated were between 18 and 45 years old. The mean maternal age at termination was  $31.38 \pm 6.30$ . The number of pregnancy of women was between 1 and 7, and the number of births was between 0 and 5. It is noteworthy that the average number of pregnancies is  $2.22 \pm 1.34$  and the average number of births is  $0.80 \pm 0.85$ . Regarding this, situations such as the spontaneous abortion of these women before, fetal anomalies or any reason for normally delivery time could not be reached, may come to mind here. However, none of the women included in the study had a history of termination of pregnancy due to fetal anomaly. The mean fetal weight, which was measured after termination, occurred to be  $215.76 \pm 137.8$  grams (range 50 to 900). All demographic and clinical characteristics of pregnancies were demonstrated in Table 1. We have also classified pregnancy terminations according to all indications according to age range, 116 (36.4%) aged 30-34,  $\geq 29$  age 111 (34.9 %), 53 (16.6 %) aged 35-39 and  $\geq 40$  age 38 (11.9%) respectively. We found that most terminations occurred in the 30-34 age range (36.4%) Table 2. Fetal congenital, chromosomal and obstetrical indications were in 308 (96.8%), and maternal indications were in 10 (3.2%) of evaluated 318 pregnancies. In our study, the most frequently detected anomalies whose termination was required were detected as central nervous system and chromosome anomalies. On the other hand, due to the spontaneous and premature rupture of the membranes even though there was no anomaly, the number of pregnancies required to be induced for termination was also considerably higher. It was not surprising for us that the most detected chromosomal anomaly was trisomy 21. On the other hand, the most frequently observed indication for maternal reason was drug use which is undoubtedly a remarkable finding. This may be due to absence of some complications as diabetes or preeclamptic. All these maternal and fetal indications and chromosomal anomalies are shown in Table 3 and Table 4 in detail.

### 4. Discussion

Fetal malformations are one of the leading causes of perinatal mortality. Fetal abnormalities cause significant permanent health problems and impose a major health burden [12].

Widespread use of routine prenatal screening tests parallel to changes in universal prenatal screening policies and technological advances in USG made it easy to diagnose the possible fetal malformations. This condition also leads to increased TOP rates. Gestational ages, presence of severe or

**Table 2. Distribution of indications of termination of pregnancy by age range.**

Age Range	≤ 29	30-34	35-39	≥ 40	Total
Central nervous system anomalies	28	35	10	6	79
PPROM (< 23 w)	21	11	6	4	42
Multiple fetal anomalies	8	11	4	4	27
Anhydramnios (without congenital anomalies)	7	10	3	1	21
Cardiovascular system anomalies	9	7	2	2	20
Genitourinary system anomalies	8	4	1	1	14
Musculoskeletal system anomalies	7	4	2	1	14
Cystic Hygroma	3	2	1		6
Hydrops Fetalis	2	2	1		5
Thoracic anomalies	1	1			2
Use of X group drugs (methotrexate etc.) during pregnancy	1	2	2		5
Advanced stage malignancies			1	1	2
Cardiovascular and Renal diseases		1			1
Congenital metabolic liver diseases		1			1
Maternal fetal infections	1				1
Trisomy 21	6	10	12	11	39
Trisomy 18	2	5	3	6	16
Triploidy	1	3	1		5
Turner syndrome	2	1	1		4
Trisomy 13		1	2		3
Monosomy X	1	1	1		3
Triple X syndrome		1		1	2
Duchenne muscular dystrophy	1				1
Fragile X syndrome		1			1
Di George syndrome	1				1
Partial trisomy 3		1			1
Partial 4p deletion		1			1
Partial trisomy 18	1				1
Total n (%)	111 (34.9 %)	116 (36.4%)	53 (16.6 %)	38 (11.9%)	318

PPROM = Preterm premature rupture of membrane.

fatal abnormal and/or chromosomal disorders were the most decisive factors in continuation or termination of pregnancy [9, 13]. TOP has always been discussed in terms of medical, legal, religious and ethical aspects [14]. Because of that the decision to terminate pregnancy is a critical medical procedure and therefore requires a multidisciplinary approach [15].

In our study, the most common indication for termination was central nervous system abnormalities 24.8% (mostly anencephaly and neural tube defects) among fetal structural abnormalities in accordance with many previous studies. Hern *et al.* examined 1005 cases underwent TOP for fetal abnormalities or fatal deaths, whose gestational week ranged from 12 to 39 weeks and they found that the most common structural abnormalities (n = 494) were neural tube defects and central nervous system abnormalities (n = 252) [9, 13, 15, 16]. Other detected CNS abnormalities were acrania, anencephaly and encephalocele which was high in first trimester. Our second mostly detected TOP indication was chromosomal disorders 24.5% (trisomy 21 in 12.3%, trisomy 18 in 5%, trisomy 13 in 0.9%, triploidy in 1.6%, Turner syn-

drome in 1.3%, triple X syndrome in 0.6%, Duchenne muscular dystrophy in 0.3%, fragile X syndrome in 0.3%, Di George syndrome in 0.3%, partial trisomy 3 in 0.3%, 4p partial deletion in 0.3%, partial trisomy 18 in 0.3% of chromosomal disorders group).

Kiver *et al.* reported that chromosomal disorders (trisomy 21 with 15.5%) were the most common indication of TOP in 1746 cases terminated > 14 weeks for maternal and fetal indications [17]. In our study, we found similarly with previously reports that chromosomal disorders constitute the most common indication for TOP, followed by central nervous system abnormalities [9, 15–21].

We found that PPRM was the third most common indication of TOP after structural and chromosomal abnormalities with a rate of 13.2%. We attributed this to study at a university hospital-tertiary center, with perinatology and neonatal intensive care units, and high referral rates in early gestational weeks. This was a study previously reported from Turkey, Baran *et al.* reported PPRM as the most common TOP indication [22].

**Table 3. Termination indications of pregnancy.**

	Total	
(a) Fetal congenital, chromosomal and obstetrical reasons (number (percentage))	308 (96.8%)	Average gestational week at termination (Min-Max)
Central nervous system anomalies	79 (24.8%)	19 (12-30)
Chromosomal disorders	78 (24.5%)	19 (12-30)
PPROM (< 23 w)	42 (13.2%)	18 (16-23)
Multiple fetal anomalies	27 (8.4%)	19 (12-24)
Anhydramnios (without congenital anomalies)	21 (6.6%)	18 (15-23)
Cardiovascular system anomalies	20 (6.2%)	21 (18-29)
Genitourinary system anomalies	14 (4.4%)	17 (16-21)
Musculoskeletal system anomalies	14 (4.4%)	19 (15-31)
Cystic Hygroma	6 (1.8%)	15 (12-23)
Hydrops Fetalis	5 (1.5%)	17 (15-26)
Thoracic anomalies	2 (0.6 %)	22 (22-22)
(b) Maternal reasons	10 (3.2%)	
Use of X group drugs (methotrexate etc.) during pregnancy	5 (1.5%)	12 (12-19)
Advanced stage malignancies	2 (0.6%)	18 (14-22)
Cardiovascular and Renal diseases	1 (0.3%)	20
Congenital metabolic liver diseases	1 (0.3%)	22
Maternal fetal infections	1 (0.3%)	13
Total	318	18

PPROM = Preterm premature rupture of membrane.

**Table 4. Distribution of chromosomal anomalies among all indications.**

	Number of patients	Percentage
<b>Chromosomal disorders</b>		
Trisomy 21	39	12.3%
Trisomy 18	16	5%
Triploidy	5	1.6%
Turner syndrome	4	1.3%
Trisomy 13	3	0.9%
Monosomy X	3	0.9%
Triple X syndrome	2	0.6%
Duchenne muscular dystrophy	1	0.3%
Fragile X syndrome	1	0.3%
Di George syndrome	1	0.3%
Partial trisomy 3	1	0.3%
Partial 4p deletion	1	0.3%
Partial trisomy 18	1	0.3%
Total	78	

All PPRM cases in our study were isolated PPRM cases below the viability limit (< 23 weeks), diagnosed with chorioamnionitis or developing anhydramnios, without additional structural and genetic abnormalities. Isolated anhydramnios cases without congenital structural abnormalities were included in the anhydramnios group. Multiple fetal abnormalities, cardiovascular system abnormalities, anhydramnios (without isolated congenital abnormalities), genitourinary system abnormalities, musculoskeletal abnormalities, cystic hygroma, hydrops fetalis and thoracic abnormalities were observed less frequently.

According to the German Federal Statistical Office data, the TOP rate has decreased in the last two decades, but there has been an increase in the termination rates above the viability limit. It was stated that only early screening of maternal and fetal conditions can considerably prevent pregnancy terminations above the viability limit [17]. Fetal viability is defined as the point at which the fetus can survive independently of pregnancy. The Royal College of Obstetrics and Gynecology (RCOG) defines the viability limit as 23<sup>+0</sup>-24<sup>+6</sup> weeks of gestation [23, 24].

The mean termination week of our cases was 18 weeks and 90% of the terminations were performed before 23<sup>+0</sup> weeks of gestation. Ten percent of TOP cases were performed by intrauterine feticide procedure after > 23<sup>+0</sup> weeks of gestation. Our results were found to be close to large-scale studies in Turkey (6.4%) and U.K. (8.4%) [15, 25, 26].

However, in the presented study, termination rates were found to be considerably lower than the studies found by Tayyar *et al.*, by Gedikbasi *et al.* [18, 27].

Legal regulations of every country determine the principles of TOP according to range of gestational weeks and maternal, fetal and other specific criminal-cultural indications. These regulations are arranged under family planning regulations in Turkey [8, 9]. In 43 states of the USA, TOP is prohibited after a certain week of gestation (mostly within the limits of fetal viability), except when it is vital for the women's life. In many European countries, it is possible to terminate the pregnancy in the early gestational weeks (usually up to 12 weeks) and in some special cases it allows the termination of pregnancy in the following weeks. While in Iran, pregnancy



can be allowed for up to 16 weeks if maternal life is at risk or if there are fetal problems, in Ireland and Malta, which are European countries, termination is prohibited regardless of gestational week except in cases that threaten the life of the mother [27, 29]. TOP up to 10 weeks of pregnancy is legal in Turkey with the couple's request. In cases of gestational week more than 10 weeks, termination of pregnancy can be made by two physicians' decision, regardless of gestational week, in cases where the continuation of pregnancy threatens the life of the mother and/or in cases of fatal or incurable chromosomal and congenital structural abnormalities that may cause serious problems in the fetus [8, 9].

In 42 states of the USA, Belgium, Denmark, France and Italy the physician has the right to refuse medical TOP. In Turkey, there is no right of conscientious refusal to process of the physician or health care workers under the law because of religious reasons or pregnancy termination [29]. These situations sometimes hinder physicians in their decisions to terminate [5, 15]. In the method used in termination of pregnancy, the College of Obstetricians and Gynecologists recommends that women should be offered a choice for a medical or surgical termination whenever possible [30].

Although the gestational week varies according to the previous uterine surgery and the patient's history, the first trimester terminations are mostly performed by dilatation curettage method, while the second trimester terminations include systemic or local drugs, cervical dilators such as Foley balloon, dilatation extraction, intraamniotic medication, hysterotomy and hysterectomy [31]. Both medical and surgical methods can be used for second trimester pregnancy termination (after 12 weeks of gestation). First, mifepristone and misoprostol are preferred. Misoprostol can be effectively used alone if mifepristone is not available. Dilation and evacuation (D&E) is a safe surgical choice, especially if adequate cervical dilatation is achieved [32]. Since all our cases were over 10 weeks, misoprostol was used as the first choice. Foley balloon dilatations, cervical dilators (Dilapan-S<sup>R</sup>) were used in patients who did not respond to these and hysterotomy and hysterectomy were not performed in any case.

Since fetal abnormalities are one of the leading causes of perinatal mortality, early diagnosis of these pregnancies is very important. It is important for countries to establish and standardize national fetal abnormality screening programs and to implement routinely first trimester combined screening test (NT + PAPP-A + beta-hCG), second trimester screening test (inhibin-A + beta-hCG, estradiol,  $\alpha$ -Fetoprotein) and fetal abnormality screening by USG. Indications, procedures and medico-legal regulations of TOP vary between countries. These variations sometimes leave physicians in a dilemma. In cases that are incompatible with life or may cause severe disability in future life, it is important to elucidate the parents in detail and to present the termination option of pregnancy to families.

## Author contributions

SSD designed the research study. SSD, EC performed the research. SSD, EC and SA analyzed the data. SSD wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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## Conflict of interest

The authors report no declarations of interest.

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