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Clinical and genetic aspects of termination of pregnancy; tertiary center experience

Gebelik terminasyonlarında klinik ve genetik yönler; tersiyer merkez deneyimi

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Abstract

Objective: The aim of the study was to retrospectively analyze the indications Techniques and complications of pregnancy termination performed in a tertiary center.

Materials and Methods: All cases between 10 and 33 weeks of gestation between January 2021 and June 2023 were retrospectively analyzed. The patients were divided into two groups as group 1 with 11+0 to 21+6 gestational weeks and group 2 for those at 22+0 and 33+0 gestational weeks.

Results: A total of 568 pregnancy terminations were included in the study. Among all terminations the most common fetal indications were central nervous system anomalies (148 cases, 26%) and trisomy 21 (53 cases, 9%) and the most common maternal/obstetrical Indication was previable premature rupture of the membranes (179 cases, 31.5%). Abnormal genetic results were found in 50 of 173 cases (28.9%) with a termination indication of Structural malformation who accepted invaziv genetic testing. The number of terminations with

fetal indications performed after 22 weeks were 148 (41%) and 11 (7.4%) cases of these late terminations of pregnancy were anomalies expected to be diagnosed in the first trimester. Complication rates (12.4%) and abdominal termination rates (3.5%) were significantly higher in group 2 than in group 1 ($p<0.05$).

Conclusion: Improvements in prenatal genetic screening and diagnostic techniques will undoubtedly decrease the gestational ages in terminations of pregnancies. However, there will always be cases that can neither be diagnosed earlier nor can be treated due to the nature of the anomaly. In the management of such cases, terminations will always occupy an important place in prenatal care.

Keywords: Fetal ultrasonography, congenital anomaly, pregnancy complications, prenatal diagnosis

Öz

Amaç: Bu çalışmanın amacı üçüncü basamak bir merkezde gerçekleştirilen gebelik terminasyonu endikasyonlarını, tekniklerini ve komplikasyonlarını retrospektif olarak değerlendirmektir.

Gereç ve Yöntemler: Ocak 2019 ile Ağustos 2022 arasında 10 ila 33. gebelik haftaları arasındaki tüm olgular değerlendirildi. Hastalar; 11+0 ile 21+6 gebelik haftaları arasındakiler grup 1 ve 22+0 ile 33+0 gebelik haftaları arasındakiler grup 2 olmak üzere iki gruba ayrıldı.

Bulgular: Çalışmaya toplam 568 gebelik terminasyonu dahil edildi. Tüm terminasyonlar arasında en sık görülen fetal endikasyonlar merkezi sinir sistemi anomalileri (148 olgu, %26) ve trizomi 21 (53 olgu, %9) iken en sık görülen maternal/obstetrik endikasyon ise previable preterm erken membran rüptürüydü (179 olgu, %31,5). Genetik testi kabul eden terminasyon endikasyonu yapısal malformasyon olan ve invaziv genetik tanı testi yaptırmayı kabul eden 173 olgunun 50'sinde (%28,9) anormal genetik sonuç saptandı. Yirmi iki haftadan sonra fetal endikasyonla yapılan gebelik terminasyonu sayısı 148

PRECIS: We evaluated terminations of pregnancy after 10th gestational week, performed in a 2.5 year period, in terms of indications, timing, process and complications.

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(%41) olup, bu geç terminasyonların 11'i (%7,4) ilk trimesterde saptanması beklenen anomalilerdi. Grup 2'de komplikasyon oranları (%12,4) ve abdominal terminasyon oranları (%3,5) grup 1'e göre anlamlı olarak yüksekti (p<0,05).

Sonuç: Prenatal genetik tarama ve tanı tekniklerindeki gelişmeler, gebelik terminasyonlarının daha erken gebelik haftalarında yapılmasını sağlayacaktır. Ancak doğası gereği erken teşhis edilemeyen veya tedavi edilemeyen olgular her zaman olacaktır. Bu tür olguların yönetiminde gebelik terminasyonları, doğum öncesi bakımda her zaman önemli bir yer tutacaktır.

Anahtar Kelimeler: Doğumsal anomaliler, fetal ultrasonografi, gebelik komplikasyonları, prenatal tanı

Introduction

Termination of pregnancy (TOP) is a medical procedure performed to terminate undesired pregnancies, pregnancies with maternal life-threatening morbidity or fetal incurable anomalies potentially leading to serious sequelae. Advances in prenatal genetic diagnosis and fetal imaging technologies as well as the widespread use of routine prenatal screening programs have made it possible to diagnose many fetal abnormalities during the antenatal period. Despite advances in fetal medicine and fetal therapies as well as postnatal therapies, TOP still occupies an important place in prenatal care due to limited treatment options for many congenital anomalies.

In Turkey, until the 10th gestational week, the pregnancy can be terminated at the request of the parents. After the 10th week, the pregnancy can be legally terminated due to a life-threatening maternal condition or a fetal abnormality that will lead to a serious outcome (Family planning law no: 2827, May 27, 1982). Therefore, TOP is frequently performed medically regardless of the gestational week, especially in tertiary centers. In this report, we retrospectively evaluated the indications, procedures, and complications of terminations between 11 and 33 weeks of gestation.

Materials and Methods

This study was conducted retrospectively at University of Health Sciences Turkey, Zeynep Kamil Women and Children Diseases Training and Research Hospital. All terminations of pregnancy performed due to fetal, maternal or obstetric indications beyond the 10th gestational week from January 2021 to June 2023 were evaluated. Patient demographics and clinical characteristics were derived from patient files and electronic archives. The study was approved by the local ethics committee (no: 76-2022, date: 22.06.2022 - University of Health Sciences Turkey, Zeynep Kamil Women and Children Diseases Training and Research Hospital Clinical Research Ethics Committee) and it was carried out in accordance with the principles of the Declaration of Helsinki. Malformations that affect more than one organ system with unknown genetic results were considered complex malformations. Chorionic villus sampling or amniocentesis were offered and performed for genetic diagnoses in necessary cases. Congenital malformations with abnormal genetic results were grouped according to genetics results that constitute the indication for the TOP. Genetic work-up was also performed for structural anomalies incompatible with life or causing severe sequelae. These cases were considered as structural anomalies as termination indications. Genetic work-ups were not waited to conclude the TOP. Previable preterm premature the rupture of membranes cases were included in the study only if the pregnancy was actively terminated by parents request. Terminations were grouped as before and after 22 weeks, which constitutes the life expectancy limit (group 1, before 22 weeks and group 2 after 22 weeks)[1]. Each pregnancy termination request was discussed and concluded by a committee consisting of consultants from relevant departments. If a live born neonate is expected, predominantly in pregnancies after 22 weeks of gestation, the procedure was initiated by performing a feticide with intracardiac or umbilical venous potassium chloride injection[2]. Three methods were used for termination: pharmacological, mechanical, and combined. Misoprostol (PGE1) was administered according to FIGO recommended regimens[3]. Extraamniotic cervical balloon dilatation was used as the mechanical method. In some cases, mechanical dilation was combined with pharmacological agents (misoprostol/oxytocin). Hysterotomy was decided in case of complication or failure of the other termination methods depending on the patient's gestation week and uterine surgery history. The need for surgery or transfusion as a result of massive bleeding after termination was considered bleeding complications. Endometritis was diagnosed with clinical and laboratory findings. The indication for curettage was evaluated by sonographic examination after the abortion.

Statistical Analysis

The study data were analyzed using IBM SPSS statistics version 22.0 (IBM Corporation, Armonk, New York, United States. Descriptive statistical parameters such as the mean ± standard deviation, median along with 25-75% interquartile range, numbers and percentages for categorical variables were used for statistical evaluation. Kolmogorov-Smirnov test was used to test the distribution of continuous data. Independent samples t-test compared two independent gestational week-based groups where numerical variables are normally distributed. The Mann-Whitney U test is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed. The Pearson chi-square test or Fisher exact test was used to compare the differences between categorical variables were appropriate. In all statistical analyzes, the significance level (p-value) was determined at 0.05.

Results

A total of 568 pregnancy terminations were analyzed. The mean age of the patients undergoing pregnancy termination was 30.2±6.2, and the gestational week at which the termination was performed was 19.8±4.3. The current study revealed that 47.2% of pregnancy terminations were performed due to fetal structural malformations, 16.4% to genetic abnormalities and 36.4% to maternal/obstetrical indications. Table 1 shows the indications for the 568 pregnancy terminations performed. In 3 of the 93 patients who underwent TOP for a chromosomal/genetic abnormality, genetic research was carried out due to the history of a child with a genetic disease (metachromatic leukodystrophy, spinal muscular atrophy, Pompe disease). Of the remaining 90 patients, 66 (73.3%) were diagnosed with abnormal ultrasound findings and 24 (26.7%) were diagnosed with further investigations due to high risk in the first trimester screening test. The mean TOP week of the patients diagnosed through abnormal ultrasound finding was 22±3.6 whereas the mean TOP week of the patients diagnosed with a genetic

Table 1. Indications for termination of pregnancy

A. Fetal Structural Malformations (± genetic abnormalities)			**268 (47.2%)**
Central Nervous System (n=148)			
-Spina Bifida	50	-Agenezis of the corpus callosum	3
-Acrania/Exencephaly/Anencephaly	49	-Cortical developmental malformations	3
-Cephalocele	11	-Vermian agenezis/ hypoplasia	4
-Hydrocephalus	8	-Ischemic/ hemorrhagic lesions	6
-Craniorachischisis/Iniencephaly	6	-Intracranial tumor	1
-Holoprosencephaly	6	-Rhombencephalosynapsys	1
Complex Malformations (n=36)			
Cardiovascular System (n=5)			
-Right isomerism	2	Hypoplastic Left Heart (HLHS)	2
-Left isomerism	1		
Genitourinary System (n=29)			
-Bilateral Renal Agenezis	9	-Bilateral Multicystic Kidney	6
-Lower urinary tract obstructions (LUTO)	10	-Renal dysplasia	4
Abdominal and Thoracic Malformations (n=7)			
-Diaphragmatic Hernia	4		
-Abdominal wall defect§	3		
Lethal Skeletal Dysplasia (n=13)			
Fetal Akinesia Deformation Sequence (FADS) (n=6)			
Non-immun Hydrops Fetalis (n=15)			
Limb Body Wall Complex (n=9)			
B. Fetal Chromosomal/Genetic Abnormalities (± sonographic findings)			**93 (16.4%)**
Trisomy 21	53	Xq22 deletion	1
Trisomy 18	15	Trisomy 9	1
Trisomy 13	3	4p deletion (Wolf Hirschhorn)	1
Meckel Gruber	3	Metachromatic Leukodystrophy	1
Turner Syndorme (45,X0)	5	Spinal Muscular Atrophy	1
22q11 deletion (Di-George)	2	Prader Willi	1
7q11 deletion (Williams Beuren)	2	RASophathy	1
Xp22 deletion (Ichthyosis, X-linked)	2	Pompe Disease	1
C. Maternal/Obstetrical Indications			**207 (36.4%)**
Previable PPROM + Anhydramnios	179	Abnormal Placentation	8
Previable Severe FGR†	11	Hypertension	1
Embryo Reduction	7	Sexual Abuse	1
Total			**568 (100.0%)**

§: Includes exomphalos and gastroschisis, †: With pathologic fetal Doppler findings and fetal chronic hypoxia signs on ultrasound. PPROM: Premature preterm rupture of the membranes, FGR: Fetal growth restriction

investigation following high risk the first trimester screening was 19±3.3. The difference was significant (p=0.002). Genetic research was conducted in 173 of 268 structural malformations that indicate TOP. 50 (28.9%) abnormal genetic test results were detected in the structural malformations that constitute the indication for the TOP. Genetics analyses and abnormal results in structural malformations are shown in Table 2.

Indications for TOP according to gestational age are summarized in Table 3. In group 2, TOP rates due to fetal structural malformations (59.0% vs. 41.8%, p<0.001) and chromosomal/genetic abnormalities (24.2% vs. 12.8%, p=0.001) were higher than group 1. Central nervous system malformations and numerical chromosomal anomalies comprised the leading anomalies in group 2. Maternal/obstetric indication rates were higher in group 1 than in group 2 (45.4% vs. 16.8%, p<0.001). When TOP processes were compared between groups, time for family to decide on termination, duration of induction and hospitalization time was longer in group 2 than group 1 (p<0.05). There was no difference in the history of uterine surgery between groups (p=0.503). Need for hysterotomy (abdominal TOP) (3.5% vs. 0.5; p=0.001), need for combined method for vaginal termination (31.4% vs. 17.2%; p<0.001) and complication rates (12.4 vs 5.6%; p=0.005) were higher in group 2 than group 1. Ten of 11 patients who underwent

Table 2. Genetic work-ups and results of the structural malformations shown in Table 1, section A

Affected System (Patients with genetic work-up/ Total cases)	Chromosomal abnormalities/ Performed Karyotyping (n)	Microarray abornomalities/ Performed CMA (n)	Single gene disorders/ Performed Molecular Genetic Analyzes (n)	Abnormal Genetic Results / Patients with genetic work-up(%)
Central Nervous System (83/148)	**8/83** -Trisomy 18: (4) -Trisomy 13: (3) -Triploidy: (1)	**7/56** -22q11 del: (1) -Xp22 del: (1) -8p21 del : (1) -4p14 del: (1) -7q 31 del : (1) -Xq28 dup: (1) -19q13 del: (1)	**8/10** -Joubert: (1) -Caudal Regression: (1) -Coffin-Siris: (1) -Walker Warburg: (2) -Incontinentia Pigmenti: (2) -Jarcho Levin: (1)	**23/83 (27.7)**
Cardiovascular System (5/5)	**0/5**	**0/4**	**0/1**	**0/5 (0.0)**
Genitourinary System (14/29)	**2/14** -Trisomy 21: (1) -Trisomy 18: (1)	**1/7** -17q12 del: (1)	**2/3** -Nephrolithiasis/osteoporosis hypophosphatemic-1: (1) -AR PKD: (1)	**5/14 (35.7)**
Abdomen (6/7)	**0/6**	**1/5** -12p dup: (1)	**0/1**	**1/6 (16.6)**
Skeletal (12/13)	**1/12** -45X0: (1)	**0/9**	**4/6** -Achondrogenesis: (2) -Osteogenesis Imp. type 3: (1) -FGFR3 gene mutatation: (1)	**5/12 (41.6)**
Hydrops (12/15)	**2/12** -Trisomy 21: (1) -Mosaic 45X0 + trisomy 18: (1)	**0/8**	**2/3** -Achondrogenezis: (1) -PTPN-11 mut: (1)	**4/12 (33.3)**
FADS (6/6)	**0/6**	**0/4**	**2/3** -Neu-Laxova: (1) -FADS-3: (1)	**2/6 (33.3)**
Limb body wall (5/9)	**0/5**	**0/3**	**0/0**	**0/5 (0.0)**
Complex Malformations (30/36)	**5/30** -Trisomy18: (3) -Triploidy: (1) -der(5)t(5;7): (1)	**3/23** -22q11 del: (1) -16p12.2: (1) -1p36 del: (1)	2/4 -Schinzel-Giedion: (1) -Acrofacial Dysostosis: (1)	**10/30 (27.7)**
Total (173/268)	**18/173**	**12/119**	**20/31**	**50/173 (28.9)**

CMA: Chromosomal microarray, del: Deletion, dup: Duplication, der: Derivation, FADS: Fetal akinesia deformation sequence, AR: Autosomal recessive, PKD: Polycystic kidney disease, Imp: Imperfecta

Table 3. TOP indications according to gestational weeks

		Group 1 n (%)	Group 2 n (%)	p-value
Structural	CNS CVS GUS Abdominal/Thoracic Skeletal System Hydrops FADS Limb Body Wall Complex Malformations	93 3 18 4 6 11 1 9 18	55 2 11 3 7 4 5 0 18	
	Total	**163 (41.8)**	**105 (59.0)**	**<0.001**
Chromosomal/Genetic	Numerical Structural İnherited	43 3 4	34 5 4	
	Total	**50 (12.8)**	**43 (24.2)**	**0.001**
Maternal/Obstetrical		177 (45.4)	30 (16.8)	<0.001
Total		**390 (100.0)**	**178 (100.0)**	

Values given as number or numbers (percentage). CNS: Central nervous system, CVS: Cardiovascular system, GUS: Genitourinary system, FADS: Fetal akinesia deformation sequence, TOP: Termination of pregnancy

abdominal TOP and had a history of uterine surgery. Hysterectomy was performed in only two patients, one due to cesarean scar pregnancy and the other due to massive bleeding during the termination procedure. Medical method utilization for vaginal termination (79.6% vs. 59.0%; p p<0.001) and need for curettage after abortion (79.9% vs. 36.0%; p<0.001) rates were higher in group 1 than group 2 (Table 4).

Table 4. Clinical characteristics and complications of the gestational age groups†

	Group 1 (n=378)	Group 2 (n=178)	p-value
Decision time for TOP (days)	0 [0-2]	2 [0-5]	<0.001
History of uterine surgery	97 (25.7)	41 (23.0)	0.503
Termination Route Abdominal Vaginal	 2 (0.5) 376 (99.5)	 9 (3.5) 169 (94.9)	 0.001
Vaginal Termination Method Medical Mechanical Combined	 301 (79.6) 10 (2.7) 65 (17.2)	 105 (59.0) 8 (4.5) 56 (31.4)	 <0.001 0.210 <0.001
Duration of induction in vaginal terminations (days)	1.5±0.9	1.9±1.0	<0.001
Complication Bleeding Uterine Rupture Endometritis Hysterectomy	21 (5.6) 12 (3.2) 1 (0.3) 7 (1.8) 1 (0.3)	22 (12.4) 11 (6.2) 2 (1.1) 8 (4.5) 1 (0.6)	0.005
Need for Curettage	302 (79.9)	64 (36.0)	<0.001
Hospitalization time (days)	2.7±1.2	3.1±1.4	<0.001

†: 12 cases (7 embryo reductions and 5 selective fetocides due to fetal anomaly) were excluded from the table. Values given as median (Q1-Q3), number (%), mean ± standard deviation, TOP: Termination of pregnancy

Discussion

The aim of prenatal care is prediction and prevention of the maternal and fetal risks, to detect the fetal anomalies, and to provide the necessary prevention or treatment modalities to the patients. However, most fetal malformations or genetic disorders lead to serious disabilities that are currently uncurable or are known to have treatment methods with unfavourable results. Therefore, TOP may be an option for such cases. Although there is no legal upper limit of gestational weeks for TOP due to maternal or fetal indication in Turkey, according to the 2011 Ankara declaration, pregnancy termination after the 24th week is not recommended[4,5]. Therefore, it is important for reference centers to publish their termination series.

In this study, it was shown that the most common indication of TOPs was fetal structural malformations in line with the literature[6,7]. Anomalies of the central nervous system system, complex malformations and anomalies of the genitourinary system were the most frequently observed structural malformations. Chromosomal and genetic causes have also been shown as the main indications for pregnancy terminations in the reported publications[8,9]. In the current study, chromosomal/genetic abnormalities were found to be 16.4% consistent with the literature. The rate of abnormal genetic results (28.3%) was found to be quite high in genetic analyses of TOPs performed due to structural anomalies. Comprehensive genetic studies have utmost importance in fetal structural malformations to

find out the genetic etiology leading to the malformation -if exists- even if the malformation alone constitutes the indication for TOP independent of genetic results. This may reveal some of these the hereditary genetic abnormalities and provide alternatives like preimplantation genetics diagnosis or invasive prenatal diagnosis chance at earlier weeks to the couples in subsequent pregnancies, particularly in nations like ours where consanguineous marriages are widespread.

The rate of cardiovascular system anomalies in TOP indications was quite low compared to recent studies[7,8,10,11]. Since the surgical intervention for congenital heart diseases can be performed effectively in our country, the termination demand may be less for fetuses with congenital heart disease. In addition to the indications for pregnancy terminations, the timing of termination is another issue that needs to be discussed. The timing of termination is closely dependent on the gestational weeks at which the ultrasonographic or genetic diagnosis is made. Syngelaki et al.[12] reported that all cases of acrania, holoprosencephaly, encephalocele, exomphalos, gastroschisis and body stalk anomalies can be detected in the first trimester by anatomical scanning. In our series 43 of 78 cases including these anomalies were terminated after 14 weeks and 40 of them could not be diagnosed in the first trimester for several reasons. Mean diagnosis and termination weeks of these 78 cases were 15.7±3.8 and 16.4±4.2 respectively. As we realize that most of the above-mentioned cases were diagnosed in their first appeal to our center, we can advocate that sonographic basic fetal screening is lacking in primary obstetrical care centers. In addition, the mean TOP weeks in chromosomal abnormalities detected with abnormal ultrasound findings was higher than those detected by high risk in the aneuploidy screening test. Despite the earlier TOP weeks in the abnormal aneuploidy screening test group, the majority of the genetic abnormalities indicated terminations were owing to ultrasound signs. This reflects the paucity of the screening tests in our country especially considering that the majority of the cases were trisomy 21 which could have been detected by 11-14 weeks combined screening tests with 90% sensitivity. All these findings in line with the literature, major fetal abnormalities can be diagnosed earlier with a first trimester aneuploidy screening including early fetal anatomical scan[13,14].

In the literature, terminations made after the 22nd-24th week of pregnancies have been considered as late pregnancy terminations and have been reported with a frequency of 25%[6,7]. In this study, the rate of late TOPs was 31.3% (178 cases) and slightly above the reported publications. As in many studies, most of the indications in late TOPs were fetal structural anomalies that could be detected on ultrasound at earlier gestational weeks (neural tube defects, complex malformations, lower urinary tract obstructions…)[6,9,15]. For only fetal indications, the rate of late TOPs was 41% (n=148), consistent with the literature[16]. Eleven cases (7.4%) were anomalies expected to be diagnosed in the first trimester. In a study by Aslan et al.[17], the late termination rate was reported as 46.2%. Current study conducted 15 years later in the same region of Turkey found that the late the termination rate appeared to have slightly decreased. The widespread use of screening programs in Turkey may have been responsible for this decline. However, in our country, where aneuploidy screening programs are common and access to healthcare is easier, the significant portion of the above-mentioned detectable anomalies in the first trimester is still being terminated after the 22nd week. This raises questions about the sufficiency of the 11-14-week of examination. The absence of a legal upper gestational age limit for TOP in the countries where all these publications were reported including ours might be mitigating the obligation of obstetricians to make these diagnoses in earlier weeks. The upper gestational the age limit may contribute to focus the obstetricians' attention on first trimester anatomic scans which enhances the experience in the first trimester ultrasound. On the other hand, many patients were referred to our clinic on suspicion of a fetal anomaly in this study. Therefore, inadequate fetal anatomical scanning may not be the only reason for higher rates of late TOPs. High rates of pregnancies with no antenatal follow-up in particular regions, latency in application to the referral center, the time necessary to complete the prenatal genetic studies and prolongation of decision time of the families might be the other reasons for the failure in terminating these pregnancies on time. In a different region of Turkey, Can and Kaleli[18] find that in pregnancies after 22 weeks, the rate of TOP for fetal indication was 11.4%, and there were no cases in which TOP was performed after viability owing to chromosomal/genetic abnormalities. One can explain the inconsistency between these rates with socio-cultural factors differences between the regions and differences in healthcare providers' attitudes to approve late terminations in different regions.

We also observed that complications of the procedure were more frequent and the duration of hospital stay was longer in late TOPs, as the recent study reported[19]. Garofalo et al.[20] declared that the history of previous uterine surgery and advanced gestational week were the main risk factors for performing pregnancy terminations with hysterotomy. In our study, the fact that the rate of hysterotomy was higher in group 2 and that most of the patients were patients who underwent hysterotomy had a history of uterine surgery (n=10, 90.9%) supports the literature.

Maternal health in pregnancy terminations is influenced by psychological factors as well as medical procedures and complications. Posttraumatic stress disorder and depression symptoms in pregnancy terminations were reported in 44% and 28% of patients, respectively, and advanced gestational week was significantly associated with psychiatric complications[21]. Although it is recommended that psychiatrists participate in the process especially in late pregnancy terminations, what their role should be is a matter of debate[22]. In the current study, the time it took for the parents to make a TOP decision was longer

in group 2 than group 1. This situation can be interpreted as TOPs performed in the advanced gestational weeks have more psychological aspects.

Despite the abovementioned disadvantages of late TOPs, there is a group of abnormalities that can not be diagnosed in the first or early second trimesters such as cortical developmental defects, intracranial ischemic/hemorrhagic lesions, tumors, or severe FGR with fetal chronic hypoxia signs and severe maternal morbidities. It is obvious that such cases may also have severe consequences and require expensive palliative care. In addition to the moral burden that a baby with severe sequelae will bring to the family, it is inevitable that it will lead to financial victimization in countries where social assistance facilities are limited.

Study Limitations

The major limitation of the study is that genetic testing was not standardized in all patients. Genetic research could not be performed on patients who did not accept the invasive diagnostic procedure. Furthermore, since our center is a public hospital, genetic studies were carried out step by step. Therefore, the applied genetic tests differed between patients according to the indications. Results could have been different if whole genome sequencing or whole exome sequencing could be studied further. The second limitation is the fact that our center serves as a tertiary referral center may have led to patient selection bias.

Conclusion

In the near future, the hopes are in favor of outstanding improvements in fetal therapies and prevention of serious maternal morbidities leading to obligation of terminating the pregnancies. However, for the time being, one of the main goals of obstetricians should be to detect these anomalies as early as possible so that the frequency of related complications can be reduced. It seems that there is a need for termination in advanced gestational age weeks can be significantly reduced with early and adequate screening. Improvements in prenatal genetic screening and diagnostic techniques will undoubtedly decrease the costs of these facilities make them more accessible. This can result in a shift in rates of TOP indications from 'fetal structural malformations to "genetic disorders" and from late TOPs to first trimester TOPs. However, there will always be cases that can neither be diagnosed earlier or can be treated due to the nature of the anomaly. In the management of such cases, it is important that the laws allow pregnancy termination in the advanced weeks of gestation.

Ethics

Ethics Committee Approval: The study was approved by the local ethics committee (no: 76-2022, date: 22.06.2022 - University of Health Sciences Turkey, Zeynep Kamil Women and Children Diseases Training and Research Hospital Clinical Research Ethics Committee).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Ö.G.E., L.U., O.D., Design: Ö.G.E., L.U., O.D., Data Collection or Processing: Ç.Ö., Ü.T., Analysis or Interpretation: A.Ö., Literature Search: A.Ö., Writing: Ö.G.E., M.E.Ö.

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