

# Intrauterine fetal death and stillbirth: evaluations in a tertiary center

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## ABSTRACT

**Aims:** Despite routine prenatal care, intrauterine fetal death (IUFD) is unpredictable. With early diagnosis and prompt treatment of maternal and obstetric problems, IUFD may become less common. The aim of this study was to determine the prevalence of IUFD in pregnant patients in a tertiary care center.

**Methods:** A descriptive cross-sectional study was conducted at a tertiary center from January 2020 to August 2024 and was approved by the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Research Ethics Committee (Date: 08.11.2024, Decision No: 2024/318). Demographic characteristics of pregnant women, medical and obstetric complication rates, and histopathological findings of the placenta were recorded.

**Results:** IUFD was diagnosed in 137 of 20,356 deliveries (0.67%). Of these, 104 cases were included in the study. The period with the highest stillbirth rate was 28-33 weeks (36.3%), 46.2% of pregnant women gave birth for the first time and 77.9% were between the ages of 20-24. The most common maternal problems were maternal anemia (n=39, 37.5%). The most common perinatal outcomes were preeclampsia/eclampsia (n=12, 11.5%) and the rate of pregnant women without any perinatal problems was 57.7% (n=60). The caesarean section rate was 37.5% (n=39). In addition, the most common placental histopathological examinations were placental infarction (n=26, 25%).

**Conclusion:** A significant amount of IUFD can be prevented with routine prenatal care of patients and society, close monitoring of risk groups, and educating pregnant women.

**Keywords:** Fetal demise, intrauterine fetal death, perinatal deaths, stillbirth

## INTRODUCTION

The death of a fetus after the twentieth week of pregnancy is known as intrauterine fetal death (IUFD). Intrauterine death before the 24<sup>th</sup> week is called early intrauterine fetal death, and intrauterine fetal death after the 28<sup>th</sup> week of pregnancy is called late intrauterine fetal death.<sup>1</sup> Over two million pregnancies globally are affected by IUFD each year, making it one of the most prevalent unfavorable pregnancy outcomes.<sup>2</sup> Most of these IUFDs occur in low- and middle-income countries, and fetal deaths have remained roughly the same since 2019, despite most being preventable, making them a major public health concern.<sup>3,4</sup> IUFD rates are considered a clear reflection of the standards of prenatal care in that community.<sup>5</sup>

Classifying the causes of IUFD has long been a controversial issue.<sup>6</sup> Chromosome anomalies, infections, fetal anemias including alpha thalassemia, cord injuries, gastroschisis, extended preterm premature rupture of membranes, and abnormalities in the fetal structure are among the causes of intrauterine fetal death.<sup>7</sup> Hypertension, diabetes mellitus, renal disease, autoimmune disorders, placental abruption,

fetal growth restriction, rhesus isoimmunization, multiple gestation, post-term pregnancy, antiphospholipid syndromes, infections (particularly malaria and syphilis), a history of stillbirths, thrombophilias, systemic lupus erythematosus, advanced age, alcoholism, obesity, low socioeconomic status, illiteracy, smoking, and illnesses of the heart and blood systems are among the maternal associations.<sup>8</sup> Additionally, a number of problems continue after the birth of a stillborn fetus, with postpartum depression and other issues causing the cost of a stillbirth to be 10-70% more than the cost of a live birth.<sup>9</sup> It is the duty of service providers to support families, look into the reason for death, and act quickly to reduce the stillbirth rate. The global health community considers care during pregnancy and childbirth to lower the rate of stillbirth to be a key indicator of a health system's quality.<sup>10</sup>

The aim of our study was to find the incidence of IUFD to find the frequency of various risk factors associated with fetal death in a tertiary care center and to evaluate the consequences.

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## METHODS

This study was conducted at a tertiary center between January 2020 and August 2024 and was approved by the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Researches Ethics Committee (Date: 08.11.2024, Decision No: 2024/318). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Pregnant women with a gestational age of 22 weeks or more who were diagnosed with intrauterine dead fetus before the onset of labor were included in the study. All cases of IUFD referred to our clinic are routinely confirmed by fetal doppler and ultrasonography. A detailed history including the current pregnancy and past obstetric history was obtained from the hospital record system. Previously diagnosed pregnancy complications and perinatal outcomes were recorded from these examinations. The decision regarding the mode of delivery was based on clinical assessment of the progress of labor and the mother's condition. The fetus was weighed grossly. Histopathology findings of the examined placenta were included in the data. No photographs or X-Rays of the fetuses were taken after delivery. In the postpartum wards, mothers were monitored daily for maternal postpartum complications such as sepsis and length of hospital stay. Pregnant women with a gestational age of less than 22 weeks, pregnant women diagnosed with COVID-19 by polymerase chain reaction method (PCR), and those with missing examination data and histopathological data were not included in the study. Additionally, anomalous fetuses and medical termination of pregnancy were excluded from the study.

### Statistical Analysis

Data analysis was performed using SPSS version 20 software. The findings were then presented in tables using Microsoft Excel 2016. The software used for data calculation and tabulation was SPSS version 20. Using descriptive statistics. The results were discussed, and conclusions were drawn.

## RESULTS

A total of 20356 women who gave birth were retrospectively reviewed from the hospital record system. 137 (0.67%) patients diagnosed with intrauterine dead fetus were reached, 21 patients were not included in the study because placental histopathological examination was not performed, and 12 patients were not included in the study because of missing data in their files. The mean age of these pregnant women was 28.3±5.7, and the mean gestational week was 34.2±4.0. The mean birth weight was calculated as 2236.5±919.9. Among the age groups, IUFD was most frequently seen between the ages of 20-34. IUFD was most common in primiparous pregnancies and between the 28<sup>th</sup> and 33<sup>rd</sup> weeks of gestation. Regarding clinical features, the rate of maternal anemia was found to be 37.5% (n=39). Additionally, when hospital files were scanned, it was seen that more than half of the pregnant women (52.9%) (n=55) did not have prenatal care. Other demographic and clinical features are summarized in [Table 1](#). Preeclampsia was the most common perinatal outcome (11.5%) (n=12), 4 of these cases were complicated by eclampsia. The rarest is polyhydramnios at 1.9% (n=2). The cause of

intrauterine fetal death could not be explained in 60 (57.7%) of the pregnant women. In addition, 9 (8.5%) of the patients had two or more perinatal outcomes. 1 (0.1%) of the cases had four conditions: oligohydramnios, preeclampsia, abruptio placentae, fetal growth restriction. One (0.1%) of the cases had three conditions: GHT, oligohydramnios, and preeclampsia. Seven (6.7%) of the cases had two perinatal conditions, 31 (29.8%) had only one perinatal condition, and 60 (57.7%) had no perinatal conditions. More details about the distribution of obstetric complications are provided in [Table 2](#). When the placentas were examined histopathologically, although placental infarction and hematoma were found to be close in number (n=26, 25%; n=22, 21.1%, respectively), placental infarction was the most common placental pathology (n=26, 25%). Other placental histopathological findings are detailed in [Table 3](#).

**Table 1. Demographic and clinical characteristics of pregnant mothers with IUFD**

Parametres	Frequency (n=104)	Percentage
Age (years)	<20	5 4.8%
	20-34	81 77.9%
	35-39	15 14.4%
	≥40	3 2.9%
Parity	Nulliparous	26 25%
	Primiparous	48 46.2%
	Multiparous	30 28.8%
Delivery mode	Vaginal delivery	65 62.5%
	Caesarean section	39 37.5%
Gestational age (week)	22-27	6 5.8%
	28-33	38 36.3%
	34-36	22 21.2%
	37-42	37 35.6%
	>42	1 0.9%
Previous stillbirth	3 2.9%	
Prenatal care visit frequency	0	55 52.9%
	0-4	33 31.7%
	>4	16 15.4%
Fetal gender	Female	56 53.8%
	Male	48 46.2%
Maternal anemia	39 37.5%	
Associated medical illness (e.g., asthma, hypothyroidism, allergic rhinitis, chronic hypertension, type 1-2 diabetes mellitus etc.)	7 6.7%	

IUFD: Intrauterine fetal death

**Table 2. Medical and obstetric complications in pregnant mothers with IUFD**

Associated complications	Frequency (n=104)	Percentage
Unexplained <sup>a</sup>	60	57.7%
Preeclampsia	8	7.7%
Eclampsia	4	3.8%
Oligohydramnios	10	9.6%
Polihydramnios	2	1.9%
Macrosomia	4	3.8%
Abruptio Placentae	8	7.7%
Gestational diabetes mellitus	4	3.8%
Gestational hypertension	7	6.7%
Fetal growth restriction	6	5.8%
Total	113 <sup>b</sup>	108.5% <sup>b</sup>

<sup>a</sup>Cases without any perinatal problems, <sup>b</sup>The percentages are calculated based on the total number of patients (n=104), but the cumulative percentage exceeds 100% due to multiple conditions occurring in the same individuals. This table is meant to show the overall prevalence of each condition. IUFD: Intrauterine fetal death

**Table 3. Histopathological findings of the placenta**

Histopathological findings	Frequency (n=104)	Percentage (%)
Normal histopathology	17	16.3%
Placental infarct	26	25%
Placental hematoma	22	21.1%
Placental inflammation/infection	19	18.3%
Placental calcification	6	5.8%
Placental abruption	14	13.5%

## DISCUSSION

The frequency of stillbirths varies considerably depending on the country of observation, with a global rate of 18.9 per 1,000 live births. The incidence ranges from 2 per 1,000 live births in highly developed countries, such as Finland, to 7 per 1000 live births in the United States. In comparison, in less developed countries, such as Pakistan, the incidence can be as high as 47 per 1000 live births.<sup>11</sup> The decline in IUFD rates worldwide has been slower than expected, particularly due to difficulties and inequalities in access to health care in less socioeconomically developed countries.<sup>11</sup> In our study, the IUFD rate in the last four years was calculated as 0.67%. The studies have identified IUFD as a risk factor, especially in pregnant women over 40 years of age, regardless of gestational age, including term pregnancies.<sup>8</sup> Considering that chronic diseases such as diabetes and hypertension are known risk factors, it is expected that these conditions are seen at a higher rate in pregnant women over the age of 40. On the other hand, a different study concluded that intrauterine fetal death is more common in the 18-35 age group with a rate of 78.33%.<sup>12</sup> Similarly, in our study, the most common IUFD occurred in the 20-34 age group with a rate of 77.9%. We believe that the reason for this is that the majority of pregnant women (77.9%) are between the ages of 20-34, which is consistent with the profile of pregnant women in our country. There are also studies showing that IUFD rates are not high in adolescent pregnancies.<sup>13,14</sup> Similarly, there were 5 adolescent pregnant women in our study and the IUFD rate in our population was 4.8%. This rate was lower than in other age groups.

Patient parity is one of the risk factors for intrauterine fetal death, but there is no full consensus on this issue.<sup>1</sup> Some sources indicate that primiparous women are at higher risk,<sup>1</sup> while some studies indicate that the risk increases after the second or even fifth birth.<sup>1</sup> In our population, more than half of the IUFD cases (46.2%) occurred in primiparous pregnant women.

Some studies did not observe post-term intrauterine fetal death.<sup>12</sup> Similarly, in our study, only 0.9% were over 42 weeks and 36.5% were term gestation, and the majority of intrauterine fetal deaths occurred earlier than 37 weeks of gestation in 63.5%. However, in the same study, the mean gestational week of intrauterine fetal deaths was 38.5±1.14, while in our study, the mean gestational week was 34.2±4.0. We believe this is because the rate of preeclampsia in our study was 11.5%. In other studies, it was found that intrauterine fetal deaths due to preeclampsia were most common at 34 weeks.<sup>15</sup>

There are studies in the literature that conclude that male fetuses have a 10% higher risk of intrauterine fetal death than female fetuses.<sup>16</sup> In our analysis, on the contrary, female fetuses were slightly more common than male fetuses.

Even if IUFD occurs, the mother should be evaluated thoroughly when choosing the method of delivery. The American College of Obstetricians and Gynecologists recommends vaginal delivery for pregnancies resulting in intrauterine fetal death. A trial of labor is recommended even if a previous cesarean delivery has occurred; however, in cases where the risk of uterine rupture is higher, a repeat cesarean procedure is justified.<sup>1</sup> It is also important to remember that induction of labor in these cases carries a much higher risk of uterine rupture than in cases where labor is initiated after a previous cesarean delivery with a viable fetus.<sup>12</sup> In our study, vaginal delivery was 62.5%, while the cesarean section rate was 37.5%. Cesarean section procedures were needed due to reasons such as placental abruption and bleeding, fetal malpresentation, fetal macrosomia, and unsuccessful vaginal delivery induction.

In the literature, a number of maternal diseases have been associated with an increased risk of intrauterine fetal death. A higher incidence of this occurrence has been consistently associated with diabetes and hypertensive diseases.<sup>1</sup> They were also the most common among the patients in our study. Chronic or gestational hypertension during pregnancy is known to increase the risk of placental abruption and uteroplacental circulation problems.<sup>17</sup> It has long been known that diabetes during pregnancy increases the risk of fetal death.<sup>17,18</sup> The pathophysiological mechanism by which inadequate glycemic control leads to fetal death is mostly represented by metabolic problems that increase oxidative stress, cardiac disorders and placental vascular pathology.<sup>17,18</sup> Studies have shown that fetal death occurs most frequently in full-term pregnancies in these patients, regardless of whether the diabetes is present before or during pregnancy, with the highest risk in patients with pregestational diabetes and in all patients with poor glycemic control during pregnancy, especially in the third trimester.<sup>18,19</sup> It is of great importance to note that the conditions mentioned are preventable. Pre-pregnancy counseling, appropriate therapy, lifestyle changes and regular monitoring can prevent the complications of diabetes and hypertension or even prevent the development of the diseases in some cases.

Histopathological findings of the placenta are increasingly discussed in studies on intrauterine fetal death.<sup>20</sup> Various studies show that pathological changes found in the placenta are considered to be the cause or at least a contributing factor in fetal death in up to 60% of cases.<sup>20</sup> In our study, this percentage was even higher-up to 83.7% of placentas had some pathological findings. This may occur due to parenchymal thrombosis and placental infarction, infections or vascular occlusions.<sup>21</sup> In our study, evidence of placental infarction was found in 25% of cases, which is similar to the 27% rate reported in the literature.<sup>21</sup> In the literature, data on the frequency of chorioamnionitis in cases of intrauterine fetal death in term pregnancies vary greatly, from 10-15% to almost 30%.<sup>1,21,22</sup> In our study, evidence of infection was found in

18.3% of cases. We believe that the susceptibility to infections in some conditions, such as diabetes and anemia, contributes to this rate.

Approximately 1% of pregnancies are complicated by placental abruption, and it is reported to cause fetal death in 10-20% of cases.<sup>1,23</sup> Due to the subclinical presentation of the condition, placental abruption is primarily diagnosed clinically, but in some cases, diagnosis can only be made by histological examination of the placenta.<sup>23</sup> In our study, 7.7% of the pregnant women clinically presented with placental abruption, while this rate was found to be 13.5% in histopathological examination. This shows that the number of subclinical placental abruption cases is remarkable.

### Limitations

It should be noted that in order to draw valid conclusions about the quality of prenatal care in our region, a comprehensive review of intrauterine fetal death data in pregnancies, including fetal autopsies, is necessary. Furthermore, a limitation of this study is that it is primarily descriptive and includes data from a four-year period, which makes our study population quite small and makes it difficult to draw definitive conclusions. Another limitation is that information on the body mass index, socioeconomic level and education level of pregnant women is unavailable in the hospital data. We believe that future studies on this subject should be prospective and include standard fetal autopsy and examination of the placenta and umbilical cord by pathologists who specialize in obstetrics.

### CONCLUSION

We believe that in order to prevent IUFD and its negative effects, public awareness should be raised about IUFD risk factors, the quality of prenatal care should be improved, education on the birth and pregnancy process should be increased, and participation in these trainings should be encouraged to reduce treatment delays.

### ETHICAL DECLARATIONS

#### Ethics Committee Approval

The study was carried out with the permission of the Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Scientific Research Ethics Committee (Date: 08.11.2024, Decision No: 2024/318).

#### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

#### Referee Evaluation Process

Externally peer-reviewed.

#### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

#### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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