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Intrauterine deaths — an unsolved problem in Polish perinatology

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ABSTRACT

Objectives: The Polish criteria for "intrauterine death" include fetal demise after 22 weeks of gestation, weighing > 500 g and body length at least 25 cm, when the gestational age is unknown. The rate of fetal death in Poland in 2015 is 3:10,000. In 2020, 1,231 stillbirths were registered.

Material and methods: An analysis using 142,662 births in the period between 2015–2020 in 11 living in Poland. The first subgroup was admitted as patients > 22 to the beginning of the 30^{th} week of pregnancy (n = 229), and the second from the 30th week of pregnancy inclusively (n = 179). In the case of women from both subgroups, there was a risk of preterm delivery close to hospitalization.

Results: It was found that stillbirth in 41% of women in the first pregnancy. For the patient, stillbirth was also the first in his life. The average stillbirth weight was 1487 g, the average body length was 40 cm. Among fetuses up to 30 weeks, male fetuses are born more often, in subgroup II, the sex of the child was usually female. Most fetal deaths occur in mothers < 15 and > 45 years of age.

Conclusions: According to the Polish results of the origin of full-term fetuses > 30 weeks of gestation for death in the concomitant antenatal, such as placental-umbilical and fetal

hypoxia, acute intrapartum effects rarely, and moreover < 30 Hbd fetal growth restriction (FGR), occurring placental-umbilical, acute intrapartum often.

Key words: stillbirth; intrauterine deaths; newborn deaths

INTRODUCTION

The problem of intrauterine foetal deaths is one of the keys, and at the same time not fully explored, issues faced by specialists in maternal-foetal medicine. The final determination of risk factors and conditions in which such events occur still requires a lot of research, making it is possible to develop effective methods of prevention, stopping the unfavourable termination of pregnancy as much as possible.

Currently, according to the available literature, the term stillbirth is synonymous with foetal death before birth, and the criteria for diagnosis, including the weight of the child and its length, vary depending on the source and the recommendations applicable in a given country [1].

According to the definition of the World Health Organization (WHO), stillbirth is defined as the death of a foetus weighing more than 1,000 g or if a foetus over 28 weeks of gestation and reaching a body length of more than 35 cm [2]. The US National Center for Health Statistics defines foetal death as the delivery of a newborn with no signs of life, as indicated by no breathing, no heartbeat, no pulsation of the umbilical cord or no clear muscle movement.

There are no uniform criteria for reporting stillbirths. In Świecie, the suggested age of registered stillbirths applies to newborns after 20 weeks of gestation or later (if the gestational age is known) or a weight of at least 350 grams, if the gestational age is not known. The limit of 350 grams is the 50th percentile of weight in the 20th week of pregnancy [3].

In Poland, the term "intrauterine death" includes foetal death after 22 weeks of gestation, a weight > 500 g and body length of at least 25 cm, when the gestational age is unknown [4]. Foetal demise > 22 weeks of gestation may refer to early pregnancy (completed 22 weeks to 27 + 6 weeks) and late pregnancy (completed 28 weeks).

There are nearly two million stillbirths worldwide every year. It is estimated that, on average, 1 child dies every 16 seconds. The above figures are based on WHO and UN reports. It is important to remember that behind these statistics lie the tragedies of women and their families. The result of these traumatic experiences may be severe depressive episodes not covered by psychological assistance within the framework of regional or global healthcare financing programmes [5].

More than 40% of all intrauterine deaths occur during childbirth. These are events that could often have been avoided due to routine monitoring of the course of pregnancy, especially those high-risk. This should be done, according to specific standards, continuous work on improving the quality of perinatal care and, what is extremely important, quick access to obstetric care in cases requiring urgent intervention [6]. One of the most common causes of stillbirth is preterm birth. Intrauterine foetal death may be the result of complications related to the course of pregnancy, delivery, intrauterine infection, placental insufficiency or maternal diseases: arterial hypertension, diabetes and/or smoking. Foetal defects are the cause of no more than 10% of stillbirths [7].

The causes of foetal death can be divided into foetal (genetic factors, non-immune hydrops fetalis, infection and multiple pregnancy), placental [premature rupture of membranes, premature separation of the placenta, abnormal implantation and placental failure, umbilical cord collision and (twin to twin transfusion syndrome) TTTS syndrome], maternal (uterine defects, maternal age > 40 years, maternal diseases such as diabetes, thrombophilia, hypertension, kidney and thyroid diseases, uterine defects, overweightness, smoking, addiction, infection, overdue pregnancy, injuries and birth complications) and other factors (socioeconomic, low level of perinatal care and various unknowns).

It has been estimated that the number of registered stillbirths may still increase due to the difficult access to medical care caused by the COVID-19 pandemic. The role of preventive vaccinations in preventing this phenomenon is emphasized [8]. Statistically, 84% of all births occur in low- and middle-income countries. In high-income countries, the problem of intrauterine deaths mainly affects national minorities [9].

According to WHO data from 2015, the incidence of intrauterine deaths in the world is as high as 18.8:1000 of all deliveries. In the USA, this ratio is 6.25, while in European countries, it does not exceed 6. In England, Wales and Northern Ireland, the rate of intrauterine deaths is 5:1000, while in Poland, it is just over 3:1000, which is similar to France, Belgium and Hungary. Only the Czech Republic, Germany, Sweden, Norway and Finland can boast about their better perinatal care results [10].

Analysing the statistics from 2020, 1,231 stillbirths were registered in Poland. Data from the database of the Central Statistical Office include the mother's age, child's sex, place of residence and the consecutive pregnancy number [11]. So far, the problem of stillbirth has not been addressed on a large scale in the Polish literature. There are no analyses involving multicentre data. We do not have information on the most common causes of this phenomenon in recent years. The state of medical records, which could provide answers to many questions, was also not assessed.

The above information could be used to develop a Polish classification of stillbirth causes. This classification should be based on the evaluation of health, cultural and economic factors, on the verification of competence and commitment of medical personnel. It seems that a too high a percentage of stillbirths is not registered at all, and thus, parents are not issued a birth certificate. This is a significant moral and ethical problem related to the trauma of losing a child and the financial consequences of the resulting health issues. Stillbirth can be somewhat prevented by proper education of future parents and rational family planning, preconception care, including care for good health and nutrition of women at reproductive age, high quality of medical care, as well as by the appropriate level of qualifications of medical personnel and financing the system healthcare.

This study is an attempt to assess the current state of medical care in Poland in the context of stillbirths. It is to be one of the first to attempt to highlight this issue and be a step towards proposing an appropriate standard of conduct in pre- and post-conception care.

Research aim

Stillbirth is an issue that has not been addressed in Polish literature so far [4, 12]. Due to the lack of detailed data from centres across the country, it is impossible to reliably assess the causes and discuss the prevention of this phenomenon. This paper is an attempt to evaluate the quality of medical records kept at clinical centres, their completeness, and thus, the credibility of existing statistics on the incidence of stillbirths in the Polish population.

MATERIAL AND METHODS

Eleven clinical centres from all over the country participated in the study regarding the phenomenon of stillbirths in Poland. The observation covered a period of 5 years (2015–2020). Medical records of 142,662 deliveries were analysed. We found 761 cases in which the patient gave birth to a dead foetus. The criteria for exclusion from analysis were multiple pregnancy, undetermined gestational age > 22 weeks, undetermined gender of the child, lack of data on foetal weight, status after intrauterine therapy, abnormal karyotype and presence of foetal malformations. Ultimately, 408 cases were evaluated. For research purposes, this group of women was divided into two subgroups depending on the gestational age. The first subgroup included patients > 22 up to the beginning of the 30^{th} week of pregnancy (n = 229), and the second one from the 30^{th} + week of pregnancy (n = 179). In the case of women from both sub-groups, the reason for hospitalisation was the risk of pre-term delivery. Based on the classification of stillbirth causes in the prenatal period proposed by WHO (ICD-PM), 3 groups were distinguished: antenatal, perinatal and maternal diseases.

The following factors were taken into account in the analysis: maternal risk factors: high weight of the patient and high *body mass index* (BMI) before pregnancy and at the time of admission to hospital (BMI > 30), high weight gain of the pregnant woman, pregnancy and delivery number, method of delivery, post-caesarean section, intrauterine infections, gestational diabetes, pregnancy-induced hypertension, chronic hypertension, preeclampsia, HELLP syndrome, cholestasis of pregnancy and premature placental abruption. Potential foetal risk factors for stillbirth included: foetal growth disorders (SGA and FGR), intrauterine infections as well as pre- and perinatal hypoxia.

Data on the course of pregnancies were obtained based on reviewing pregnancy charts, medical history and physical examination of the hospitalised patients. The diagnosis of stillbirth was made based on confirming the absence of foetal heartbeat in ultrasound examination, and in the presence of two physicians. The decision regarding the choice of delivery route was made based on the current obstetric situation. Qualification for delivery by caesarean section was carried out in the event of a threat to the life and/or health of the pregnant woman and/or foetus, based on the current recommendations of the Polish Society of Gynaecologists and Obstetricians. Clinical cases of 408 patients who gave birth to a stillborn child in 2015–2020 were analysed. Sub-group 1 included patients with intrauterine death > 22 and < 30 weeks of gestation consisted of 229 patients — 56%. Sub-group 2 consisted of patients in whom foetal demise occurred the earliest in the 30th week of pregnancy included

179 women — 44%. Detailed data on pregnant women and newborns are presented in Table1.

Clinical characteristics of patients in both sub-groups included height, weight, prepregnancy body BMI, weight at admission and weight gain during pregnancy. Statistically significant differences were observed in terms of BMI before pregnancy (p = 0.095) subgroup I — $n = 23 \text{ kg/m}^2$, subgroup II — $n = 24 \text{ kg/m}^2$, weight at admission to hospital (p = 0.001, n = 71 kg vs 76 kg) and weight gain during pregnancy (p = 0.000, n = 6 kg vs 11 kg).

The obstetric history was also analysed. Attention was paid to the sequential number of pregnancies and childbirths, the birth of a child via caesarean section and the number of these procedures in the past, as well as the way of completing the current pregnancy in which intrauterine foetal death occurred. In the study group, stillbirths occurred in 41% of women in the first pregnancy (sub-group 1 — 43.67%, sub-group 2 — 37.99%). For the majority of patients — 52.70%, this was their first stillbirth (54.59% vs 50.27%). One-fifth of the patients (82 people) gave birth by caesarean section at least once (19.21% vs 21.23%). Stillbirth in most women was vaginal (82.84% — 87.34% vs 77.09%). This difference was of statistical significance (p = 0.006).

Assessment of stillbirth included sex, birth weight and length. The mean stillbirth weight was 1,487 g (736 g vs 2,448 g, p = 0.000) and mean body length was 40 cm (32 cm vs 48 cm, p = 0.000). Differences between sub-groups were statistically significant. Male newborns were delivered more often — 52.7%, however, in sub-group 2, the sex of the child was usually female — 53.07%. These differences were also statistically significant (p = 0.039).

Pregnancy complications were also assessed: gestational diabetes mellitus type 1 and 2, pregnancy-induced and chronic hypertension, preeclampsia, HELLP syndrome, gestational cholestasis, premature placental abruption and foetal growth disorders (SGA and FGR). Statistically significant differences were observed between sub-groups in the incidence of gestational cholestasis (0% vs 1.66%, p = 0.049) and intrauterine growth retardation (33.19% vs 17.32%). An attempt was made to analyse the causes of intrauterine deaths, based on the WHO ICD-PM classification (Tab. 2).

The incidence of particular causes of stillbirth was analysed based on the division into antenatal, perinatal and maternal factors. The observations are presented in the tables. It turned out that in the case of foetal death before delivery, in 56.62% of cases, the cause of death could not be determined (Fig. 1) (sub-group I — 53.71% vs sub-group II — 60.34%, p = 0.000). In cases where the cause of death could be identified, in sub-group 1, 59 cases (25.76%) were determined as foetal growth disorders, while in sub-group 2, foetal hypoxia occurred in 29 women (16.2%) (Fig. 2, 3). In the case of foetal death during delivery, the most common cause, both in the entire study group (2.7%) and in the first (3.06%) and second sub-groups (2.24%), was an acute perinatal event (Fig. 4, 5). It was found that in the case of foetal demise, in 45.1% of cases, no disease was found in the pregnant woman (Fig. 6) (sub-group I-1 — 44.54% vs sub-group 2 — 45.81%, p = 0.000) (Fig. 7).

DISCUSSION

In Poland, a standard of conduct in the case of stillbirth pregnancies has not yet been developed. In order to understand the causes of this phenomenon, it is necessary to analyse risk factors and the way of caring for pregnant women in these cases, and then, based on experience, available scientific studies and algorithms used at maternal-foetal medicine centres around the world, and later, draw appropriate conclusions. The basis for the development of the management algorithm is a detailed interview and paying attention to the conditions predisposing to an unfavourable obstetric outcome, as well as thorough physical examination.

The term "perinatal mortality" includes stillbirths and deaths of newborns in the first week of life, weighing at least 500 g (birth weight unknown) or born after the 22nd week of gestation, or reaching a body length of at least 25 cm (top of the skull to the heel). The perinatal mortality rate in 1999 was 10.8 per mille and then gradually decreased, reaching 4.35 per mille in 2018.

"Newborn mortality rate" is the number of neonatal deaths (from birth to 27 days after birth) per 1,000 live births. A similar trend is observed in neonatal mortality and morbidity in 2018, the mortality rate was 3.8 per mille, and the neonatal mortality rate was 2.8 per mille. [13]. The key issue for drawing clinically relevant conclusions is a large study group. Xiong et al. [14] accessed history data from 66,494 stillbirths. The observation period also covered 5 years, and the stillbirth rate was 1.9%. During this time, 6,970,032 deliveries took place.

In a 5-year follow-up by Kumar M et al. [15], a slightly higher percentage of stillbirths was shown, *i.e.*, 2.6% (1,239 out of 46,816 cases). There were 2,597 foetal deaths in England and Wales in 2021. In a 2021 report published by UK Perinatal Surveillance, stillbirth rates

decreased by 21% (from 4.20 per mille in 2013 to 3.33 in 2020). Thus, approximately 605 fewer stillbirths were recorded in 2020 [16].

In 2020, 20,854 foetal deaths were reported in the United States after 20 weeks of gestation. Since 2019, a 3% decrease has been recorded (21,478) [17]. Analysing the statistics from 2020, 1,231 stillbirths were registered in Poland [11]. Documentation from 2015–2020 at 11 maternity centres in Poland provided information on 142,662 deliveries, during which a dead foetus was born in 761 cases (0.5%). In the British Isles, 73% of intrauterine deaths involved premature infants between 22–37 weeks of gestation, and 34% of them — extremely premature infants between 22 + 0 and 27 + 6 weeks of gestation [16].

In 2020, the foetal mortality rate after 20 weeks of gestation was 5.74 per mille in the US. This did not significantly differ from the data found for 2019 (5.7/1,000). Mortality has decreased by 23% since 1990 (7.49/1,000) The rate of early foetal mortality (20–27 weeks of gestation) has remained essentially unchanged between 2019 (2.98/1,000) and 2020 (2.97/1,000). This indicator has decreased by 6% since 2014. Late foetal mortality (> 28 weeks of gestation) was 2.78 per mille in 2020, which was not significantly different from 2019 (2.73/1000). The rate of late foetal mortality has been basically unchanged since 2014 [17].

In Poland, 52% of stillbirths occurred in primiparous women (55% below 30 weeks of gestation, *i.e.*, in group 1, and as much as 50% above 30 weeks of gestation, *i.e.*, group 2). With each subsequent pregnancy, the risk of stillbirth decreased (26% vs 27% stillbirth during the 2nd delivery, 13% vs 15% in the 3rd delivery). The majority of stillbirths were vaginal, 87% < 30 weeks of gestation, 77% > 30 weeks of gestation, and these were predominantly male foetuses < 30 gestation weeks (57.2% comprised males). On the other hand, girls died significantly more often > 30 weeks of pregnancy (53% of deaths in females vs 46.9% in males).

Similar results are presented by statistics from the United States. Male foetuses died 5% more often than that of female, regardless of gestational age (5.88 vs 5.59 per mille) [17]. The greatest number of foetal deaths concerned mothers < 15 and > 45 years of age (13.42 vs 12.20 per mille), *i.e.*, three times more than in women aged 15–45.

In the USA, deaths in twin pregnancies were 2–3 times more frequent (12.12 per mille) than in single pregnancies (5.51 per mille) [17]. In Great Britain, there has been a 12%

reduction in foetal deaths from twin pregnancies since 2016 [16]. In Great Britain, the highest infant death rate per 1,000 births (8.1 per mille) concerned children of black mothers [16].

In the United States, black women are more than twice as likely to stillbirth than their white counterparts. However, the reasons for this phenomenon are not entirely clear. They are most likely to be found in frequent infections. Black women usually miscarry < 24 weeks or endure stillbirth [18, 19].

According to 2017 data from the CDC (Centre for Disease Control), there are large differences in stillbirth rates between different ethnic groups. These are the rates per 1,000 live and stillbirths: non-Hispanic blacks — 10.32, American Indians, Alaska Natives — 7.22, Hispanics — 5.01, non-Hispanic whites — 4.89, Asians — 4.29 [20].

Women who had experienced financial, emotional or other personal stress in the year before giving birth were at a greater risk of experiencing a stillbirth. Smoking tobacco or marijuana, taking painkillers or using illicit drugs during pregnancy is associated with a 2- to 3-fold risk of stillbirth [16–18].

In our analysis, it was found that the BMI of a mother carrying a dead foetus did not differ whether the foetal death occurred < 30 Hbd (mean BMI 23) or > 30 Hbd (mean BMI 24). The average body mass at admission to hospital was 73 kg (71 kg in group I1 vs 76 kg in group 2), and weight gain during pregnancy was < 6 kg in group 1 and 11 > in group 2. In foreign analyses, foetal death was much more common in overweight and obese mothers. The cause of death was determined in 43.38% of stillbirth cases, in the majority of full-term pregnancies (46%).

Although the percentage of stillbirths for unknown reasons has decreased, it is still the largest group of deaths in the UK, USA and Poland (as much as 33% of deaths, *i.e.*, 1.08 per mille). The SCRN (Stillbirth Collaborative Research Network) analysed over 500 cases of stillbirths that took place at 59 medical centres in the United States over a period of 2.5 years. In almost a quarter of these cases, scientists were unable to determine the probable or even possible cause of foetal death. In addition, many stillbirths had more than one probable cause.

The probable causes and contributing factors of stillbirth identified in this study are listed below in order from those most to least common:

1. Complications with pregnancy and childbirth. These caused almost every third stillbirth. These complications included preterm delivery, twin and triplet pregnancies, and premature placental abruption. Complications related to pregnancy and childbirth were more frequent causes of stillbirths before 24 weeks.

2. Almost a quarter of stillbirths were probably caused by problems with the placenta: incorrect implantation or too small placental exchange area. Deaths usually occurred after 24 weeks of gestation.

3. Birth defects of the foetus. In more than 1 in 10 stillbirths, the foetus had a genetic or structural birth defect that likely caused its death.

4. In more than 1 in 10 stillbirths, the death was probably due to foetal or placenta infection, or a serious infection in the mother. Infections were a more frequent cause of foetal deaths < 24 weeks of gestation. Bacterial infections caused by group *B streptococci*, *E. coli*, *Klebsiella*, *Enterococci*, *Haemophilus influenza*, *Chlamydia* and *Mycoplasma* or *Ureaplasma* constituted the largest group.

5. Umbilical cord complications — true knot, long or short umbilical cord being the cause of stillbirth, which is more common at the end of pregnancy.

6. High maternal blood pressure — whether from chronic hypertension or preeclampsia — this also contributed to stillbirths. These types of stillbirths were more common towards the end of the 2nd trimester and the beginning of the 3rd one.

7. Maternal chronic diseases, such as diabetes, were considered a probable or possible cause in less than 1 in 10 stillbirths.

In Great Britain, placental causes accounted for just over a third of foetal deaths (35% — 1.16 per mille). Foetal defects accounted for 0.5 per mille, while all foetal causes (CODAC — Causes of Death and Associated Conditions) accounted for 0.65–0.74 per mille of deaths over 22 weeks of gestation [15, 16].

According to the Polish experience, among full-term foetuses > 30 weeks of gestation, the overwhelming majority of deaths were due to antenatal causes, such as placental-umbilical (21.9%) and acute foetal hypoxia (16.2%), rarely acute peripartum events (2.24%), while < 30 Hbd FGR (25.76%), placental-umbilical causes (25%) and acute intrapartum events much less frequently (3.06%).

Analysing maternal causes and chronic diseases, premature placental abruption is a moderately frequent cause of death of mature and immature foetuses (9.5% in group 1 vs 6.11% in group 1).

Fetal Growth Restriction was much more often the cause of foetal death < 30Hbd (33.19 in group 1 vs 17.32% in group 2). Diet-compensated gestational diabetes more often concerned deaths of more mature foetuses, > 30 Hbd (6.15% in group 2 vs 3.93% in group 1), gestational diabetes with insulin therapy in similarly mature foetuses (1.75% in group 1 vs 5.59% in group 2).

Pregnancy-induced hypertension was more common in more mature foetuses (8.38% in group 2 vs 4.8% in group 2) and pre-gestational hypertension in less mature foetuses (5.03% in group 2 vs 7.42% in group 1). Preeclampsia was a rare cause of death, mainly < 30 Hbd (2.23% in group 2 vs 5.24% in group 1), HELLP syndrome even rarer (0.87% in group 1) while cholestasis of pregnancy was a very rare cause of death only in mature foetuses (1.66% in group 2).

CONCLUSIONS

The phenomenon of stillbirth is a huge problem, both in the diagnostic and therapeutic context. The presented data clearly show how important meticulousness is in keeping medical records. Without a thorough physical examination and additional tests, it is not possible to detect or prevent the causes of stillbirths. Given the complexity of this problem, an algorithm should be developed taking the following factors into account: patient age (< 20 years and > 40 years), socioeconomic status, place of residence within the context of distance to hospitals, including clinical centres with the highest level of reference, level of health awareness among pregnant women in the area of pregnancy and perinatal preventative measures and the quality of health care, including perinatological and obstetric care.

The foetal mortality rate is decreasing every year. At the greatest risk are women < 15 and > 45 years of age, primiparous, with first pregnancy, especially having twins, of black race, burdened with chronic diseases, smoking, addicted to drugs and marijuana or painkillers, especially < 30 Hbd. The risk of foetal death is related to the mother's race. The risk of foetal death is highest for blacks and the lowest for Asians.

The most common causes of death in the 1st trimester are chromosomal defects of the embryo (aberrations) and infections, in the 2nd trimester infections, birth defects and maternal diseases, while in full-term pregnancies, chronic maternal diseases, preeclampsia, gestational diabetes and pregnancy-induced hypertension as well as complications related to the delivery itself. In the case of stillbirth, it is crucial to collect a detailed history of the mother's health, as

well as to conduct additional examinations of the patient, foetus and postnatal. In Figure 8 presented below, a proposed diagnostic algorithm aimed at determining the cause of stillbirth is given.

As earlier mentioned, morphological assessment of the foetus is extremely important. Below is a draft chart that can help determine the cause of foetal death by assessing its anatomy. In order to understand the essence of problems related to stillbirths, a statistical database covering factors leading to intrauterine deaths should be developed and implemented, and efforts should be made to develop a reporting model on a uniform and comparable scale for other countries, in cooperation with foreign centres. It is worth following the example of the procedure proven in terms of reducing the percentage of stillbirths in other countries. According to the Australian model [13], which allowed for the lowest rate of intrauterine deaths, a national database on stillbirths should be created and funded, which would be maintained by a designated clinical unit.

In order to be able to implement the above assumptions, it is necessary to increase financial outlays on preventive programmes for the care of pregnant and postpartum patients. It is necessary to develop recommendations regarding the management of intrauterine deaths, which would present the principles of good clinical practice in this area in a clear and transparent way, based on algorithms.

Implementation of the above assumptions could contribute to a more thorough analysis of the problem and reduce its scale. Accurate statistics, detailed reporting of complications and, in particular, providing reliable medical and social care for pregnant women, could actually lead to a reduction in the number of stillbirths.

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

- 1. Metz TD, Berry RS, Fretts RC. Reddy UM, Turrentine MA. Obstetric care consensus. Management of stillbirth. Obstet Gynecol. 2020; 125(3): e110-e132.
- 2. WHO Guidance 2021: Maternal and perinatal death and surveillance and response.
- National Center for Health Statistics. Model state vital statistics act and regulations. Atlanta, GA: Centers for Disease Control and Prevention; 1992. <u>https://www.cdc.gov/nchs/data/misc/mvsact92b.pdf</u> (16.09.2019).
- Zaręba-Szczudlik J, Romejko-Wolniewicz E, Malinowska-Polubiec A, et al. Analiza czynników ryzyka zgonów wewnątrzmacicznych płodów. Perinatol Neoanatol Ginekol. 2009; 2(3): 203– 207.

- Frøen JF, Friberg IK, Lawn JE, et al. Lancet Ending Preventable Stillbirths Series study group. Stillbirths: progress and unfinished business. Lancet. 2016; 387(10018): 574–586, doi: <u>10.1016/S0140-6736(15)00818-1</u>, indexed in Pubmed: <u>26794077</u>.
- de Bernis L, Kinney MV, Stones W, et al. Lancet Ending Preventable Stillbirths Series study group, Lancet Ending Preventable Stillbirths Series Advisory Group. Stillbirths: ending preventable deaths by 2030. Lancet. 2016; 387(10019): 703–716, doi: <u>10.1016/S0140-</u> <u>6736(15)00954-X</u>, indexed in Pubmed: <u>26794079</u>.
- Lawn JE, Blencowe H, Waiswa P, et al. Lancet Ending Preventable Stillbirths Series study group, Lancet Stillbirth Epidemiology investigator group. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet. 2016; 387(10018): 587–603, doi: <u>10.1016/S0140-6736(15)00837-5</u>, indexed in Pubmed: <u>26794078</u>.
- 8. American College of Obstetricians and Gynecologists. COVID-19 Vaccination Considerations for Obstetric-Gynecologic Care. <u>https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/covid-19-vaccination-considerations-for-obstetric-gynecologic-care?utm_source=higher-</u> (15.09.2022).
- 9. Flenady V, Wojcieszek AM, Middleton P, et al. Lancet Ending Preventable Stillbirths study group, Lancet Stillbirths In High-Income Countries Investigator Group. Stillbirths: recall to action in high-income countries. Lancet. 2016; 387(10019): 691–702, doi: <u>10.1016/S0140-6736(15)01020-X</u>, indexed in Pubmed: <u>26794070</u>.
- WHO. Global Health Obrervatory data repository. Stillbirth rate. Data by WHO region. <u>https://apps.who.int/gho/data/view.main.STILLBIRTHGWHOREGIONv?lang=en</u> (15.09.2 022).
- 11. Główny Urząd Statystyczny.Baza Demografia. Wyniki badań bieżących. <u>https://demografia-.stat.gov.pl/bazademografia/Tables.aspx</u> (15.09.2022).
- 12. Troszyński M, Maciejewski T, Wilczyńska A, et al. Przyczyny martwych urodzeń i zgonów noworodków w Polsce w latach 2007–2009. Ginekol Pol. 2011; 82: 598–601.
- 13. Główny Urząd Statystyczny 2018. <u>https://stat.gov.pl/obszary-tematyczne/roczniki-staty-styczne/roczniki-statystyczne/rocznik-demograficzny-2018,3,12.html#</u> (15.09.2022).
- 14. Xiong T, Mu Yi, Liang J, et al. Hypertensive disorders in pregnancy and stillbirth rates: a facility-based study in China. Bull World Health Organ. 2018; 96(8): 531–539, doi: <u>10.2471/BLT.18.208447</u>, indexed in Pubmed: <u>30104793</u>.
- Kumar M, Vajala R, Bhutia P, et al. Factors contributing to late stillbirth among women with pregnancy hypertension in a developing country. Hypertens Pregnancy. 2020; 39(3): 236– 242, doi: <u>10.1080/10641955.2020.1757699</u>, indexed in Pubmed: <u>32396487</u>.
- 16. MBRRACE-UK Perinatal Mortality Surveillance Report for births in 2020.
- Gregory ECW, Valenzuela CP, Hoyert DL. Fetal Mortality: United States, 2020; Hyattsville, MD: National Center for Health Statistics. 2022. National Vital Statistics Reports. 2022; 71(4).
- Stillbirth Collaborative Research Network Writing Group. Causes of death among stillbirths. JAMA. 2011; 306(22): 2459–2468, doi: <u>10.1001/jama.2011.1823</u>, indexed in Pubmed: <u>22166605</u>.
- 19. Hogue CJR, Parker CB, Willinger M, et al. A population-based case-control study of stillbirth: the relationship of significant life events to the racial disparity for African Americans. Am J Epidemiol. 2013; 177(8): 755–767, doi: 10.1093/aje/kws381, indexed in Pubmed: 23531847.
- 20. CDC Center for Global Health 2017 Annual Report. <u>https://www.cdc.gov/globalhealth/resour-ces/reports/annual/pdf/CGH_Annual-Report_2017-h.pdf</u> (15.09.2022).
- 21. Khong T, Mooney E, Ariel I, et al. Sampling and definitions of placental lesions: amsterdam placental workshop group consensus statement. Archives Pathology Laboratory Med. 2016; 140(7): 698–713, doi: <u>10.5858/arpa.2015-0225-cc</u>.

	Study group n = 408		Sub-group 1 < 30 HBD n =229		Sub-grouj ≥ 30 HBD n = 179	
	Mean/N	SD/[%]	Mean/n	SD/[%]	Mean /N	SD/[%]
Height	165	6.271	165	6.475	165	5.993
Pre-pregnancy body mass	65	13.335	66	14.470	64	12.409
Pre-pregnancy BMI	23	4.607	23	4.147	24	5.118
Body mass at admission	73	14.781	71	14.083	76	76.757
Gestational weight gain-GWG	8	5.662	6	4.463	11	5.790
Foetus weight	1487	1109.169	736	459.663	2448	942.682
Foetus length	40	10.916	32	7.704	48	6.931
State after CS						
After 1	82	20.10	44	19.21	38	21.23
After 2	3	0.73	1	0.43	2	1.11
Pregnancy						
1	168	41.18	100	43.67	68	37.99
2	114	27.94	63	27.51	51	28.49
3	74	18.14	37	16.16	37	20.67
4 and more	52	12.74	29	12.66	23	12.85
Delivery			·	·		·
1	215	52.70	125	54.59	90	50.27
2	109	26.71	60	26.20	49	27.37
3	57	13.97	30	13.10	27	15.03
4 and more	27	6.62	14	6.11	13	7.26
Type of delivery			·	·		
Natural	338	82.84	200	87.34	138	77.09
Caesarean section	70	17.16	29	12.66	41	22.91
Sex of foetus			·			
Male	215	52.70	131	57.21	84	46.93
Female	193	47.30	98	42.79	95	53.07

Table 1. Clinical characteristics of the study group of patients

	Study group n = 408	,	Sub-group 1 < 30 HBD n =229	1	Sub-grouj ≥ 30 HBD n = 179	
	Mean/N	SD/[%]	Mean/n	SD/[%]	Mean /N	SD/[%]
Gestational diabetes-GDM1	20	4.90	9	3.93	11	6.15
Gestational diabetes-GDM2	14	3.43	4	1.75	10	5.59
Pregnancy hypertension-GH	26	6.37	11	4.80	15	8.38
Chronic gestational hypertension- CGH	26	6.37	17	7.42	9	5.03
Preeclampsia-PE	16	3.92	12	5.24	4	2.23
HELLP	2	0.49	2	0.87	0	0
Gestational cholestasis	3	0.74	0	0	3	1.66
Premature placental abruption	31	7.60	14	6.11	17	9.50
Diagnosed FGR	107	26.23	76	33.19	31	17.32
Diagnosed SGA	33	8.09	19	8.30	14	7.82

Pre-birtl	I Causes
A1	Congenital defects, deformities and chromosomal aberrations
A2	Infection
A3	Antenatal hypoxia
A4	Other pre-natal abnormalities
A5	Foetal growth disorders
A6	Antenatal death of unknown cause
N1	Congenital defects, deformities and chromosomal aberrations
N2	Foetal growth disorders
N3	Perinatal trauma
N4	Complications of perinatal incidents
N5	Convulsions and diseases of the central nervous system
N6	Infection
N7	Disorders of the circulatory and respiratory systems
N8	Other conditions of the newborn
N9	Low birth weight and prematurity
N10	Varied
N11	Unknown cause of newborn death

Table 2. ICD-PM classification of stillbirths causes according to WHO

Perinatal ca	uses
I1	Congenital defects, deformities and chromosomal aberrations
I2	Antenatal trauma
I3	Acute perinatal incident

I4	Infection
I5	Other perinatal causes of death
I6	Foetal growth disorders
I7	Perinatal death of unknown cause

	Mother's illness
M1	Complications of the placenta, umbilical cord and membranes
M2	Mother-related pregnancy complications
M3	Other delivery-related complications
M4	Medical and surgical conditions of the mother
M5	No determined illness of mother

Table 3. Causes of intrauterine deaths in the study group according to WHO

	Study group n = 408		Sub-group 1 < 30 HBD n = 229		Sub-group 2 ≥ 30 HBD n = 179	
	Mean/N	SD/[%]	Mean/N	SD/[%]	Mean/N	SD/[%]
Antenatal cause of death		1	<u> </u>	1	1	
A2	13	3.19	8	3.49	5	2.79
A3	46	11.27	17	7.42	29	16.20

A4	21	5.14	11	4.80	10	5.59
A5	79	19.36	59	25.76	20	11.17
A6	231	56.62	123	53.71	108	60.34
Perinatal cause of death		I				
I2	2	0.49	2	0.87	-	_
I3	11	2.70	7	3.06	4	2.24
I4	1	0.25	1	0.45	-	-
16	3	0.74	1	0.44	2	1.18
I7	1	0.25	-	_	1	0.56
Mother's illness		I				
M1	98	24.02	59	25.76	39	21.78
M2	38	9.31	24	10.48	14	7.82
M3	7	1.72	4	1.75	3	1.68
M4	81	19.85	40	17.47	41	22.91
M5	184	45.10	102	44.54	82	45.81

Control of the child's clin	nical examination	Mother's data [name, surname]
 Pregnancy: simple multiple Date of intrauterine deat 		Address PESEL number Age Mouth cavity: • correct • big
Degree of fetal maceration: • fresh (no exfoliation) • mild • small • moderate • advanced	Oral cavity: • correct • big • small Upper lips: • correct • cleft Palate Jaw	small Genitalia: Anus: correct/overgrown Sex: woman/man/untypical Man: describe penis/scrotum/testicles
Head/face: • correct • collapse • brainless • hydrocephalus • other	Ears: • correct • low-set • preauricular galls • preauricular dimpl • rotation • others	Limbs • length/shape Hands: • length • fingers (number, shape, position, fusion) Thumbs: • number • shape • position
Eyes: • correct • prominent • sunken • far-set eyes • close set eyes • oblique • big/small • close lenses/eyelids • other	Neck: Chest: • correct • long • short • wide • describe spina bifida	Fingers nails: Feet: • correct/incorrect appearance • number of nails • space between fingers • nails

Table 4. Child's world examination checklist

Nose (correct, small, big,	Abdominal:
etc.):	 correct
 obstructed 	 concave
 unobstructed 	 bloated
• single	• hernia
• other	 gastroschisis
	Back:
	 correct
	 spina bifida
	 scoliosis
	 kyphosis

Table 5. Diagnostic algorithm for proceeding in the case of death in the 2nd or 3rd trimester

1/ Research on the mother

2/ Fetal research

- 3/ Afterbirth research
- 1. Maternal Research Section:

A. Ultrasound examination with an attempt at the most accurate possible anatomical assessment of the dead fetus, AFI index, tp flow uterus and placenta

B. For a detailed obstetric history, see the diagram in Appendix A

C. Biophysical tests: weight, height, weight gain during pregnancy, blood pressure measurement

D. Laboratory tests: blood group with immune antibody test, complete blood count, CRP, general urine, fasting glucose/HbA1c, TSH, liver tests and bile acids, tests for fetal-maternal transfusion syndrome (Kleinhauer-Betke test or flow cytometry). Tests for *toxoplasmosis*, CMV, *rubella*, *Parvovirus* B19, *syphilis*, unless the results obtained earlier indicate a history of infection.

E. Toxicology tests with a history indicating a risk of using psychoactive substances

F. Tests for thrombophilia (antiphospholipid syndrome, prothrombin G20210A gene mutation test, factor V Leiden) Tests performed especially in a patient with FGR, preeclampsia, history of VTE

2. Fetal research:

A. Thorough external examination — see diagram, connector B, clinical fetal assessment card to be completed by a paediatrician, neonatologist, perinatologist

B. Securing material for genetic and microbiological research

• Cord blood, cardiocentesis — microbiological and enzymatic tests

• Umbilical cord fragment, skin fragment, blood obtained by cardiocoenthesis (depending on the collected material, degree of fetal maceration, karyotype or microarray examination)

• Autopsy examination

• Baby gram if any bone anomalies are suspected

3. Macroscopic examination of the afterbirth and microscopic assessment optimally in accordance with the Amsterdam Placental Workshop Group Consensus Statement guidelines [21]

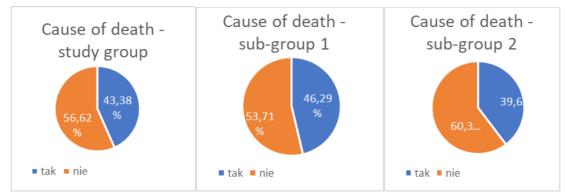


Figure 1. Determining cause of death (tak-yes, nie-no)

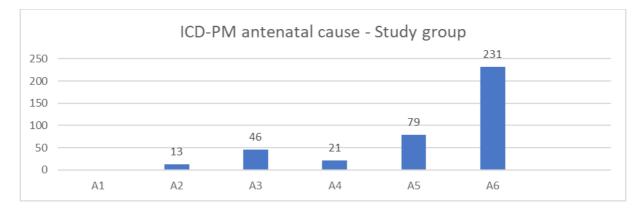


Figure 2. Antenatal causes of intrauterine deaths

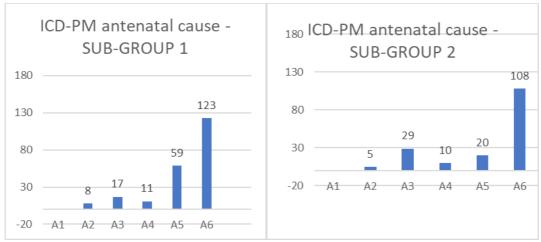


Figure 3. Antenatal causes of intrauterine deaths depending on gestational age

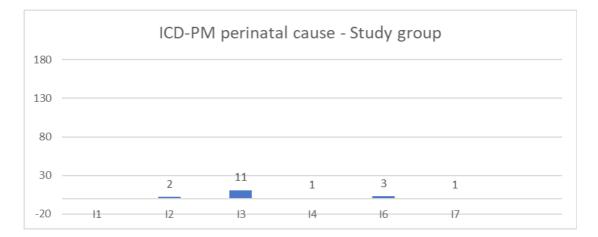


Figure 4. Perinatal causes of intrauterine deaths

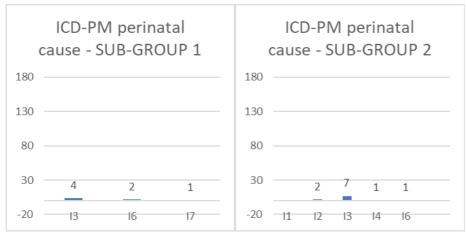


Figure 5. Perinatal causes of intrauterine deaths depending on gestational age

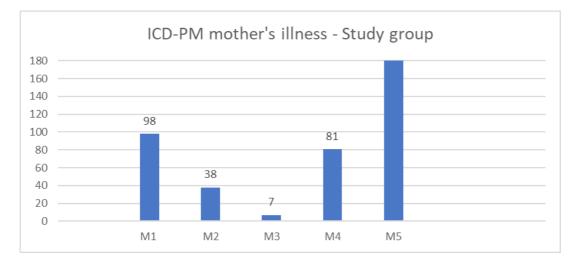


Figure 6. Maternal causes of intrauterine deaths

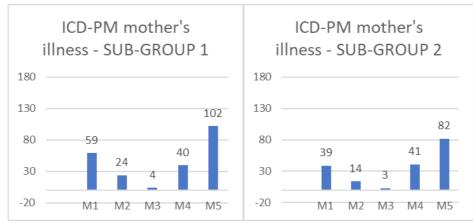


Figure 7. Perinatal causes of intrauterine deaths depending on gestational age

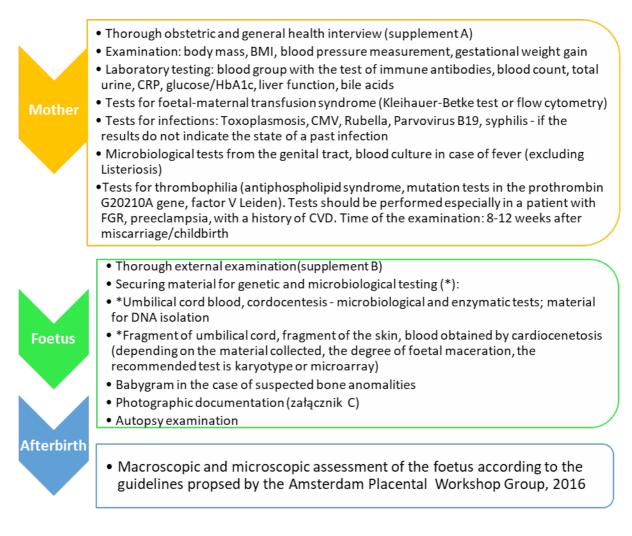


Figure 8. Diagnostic algorithm for determining the cause(s) of stillbirth