Stillbirths: An Underestimated and Neglected Reality

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Abstract

About 2.6 million stillbirths annually are estimated to occur worldwide, mainly in developing countries, although much of the data is incomplete. The aim of the present study was to analyze cases of stillbirth examined in an Institute of Forensic Medicine of the Federal District (IML-DF), Brazil. A total of 38 cases were analyzed, mostly male, with a mean gestational age of 32.9 ± 6.38 weeks. Maternal causes predominated, with hypertensive disorders during pregnancy and trauma as the leading causes; placental causes followed, the most frequent being premature detachment of the placenta. Fetal causes occurred in three cases (one of the case is cardiac malformation and two are kidney disease). In nine cases, the cause of stillbirth could not be determined. The authors call attention to the importance of stillbirth rate, which is considered one of the best indicators of quality of life in a population; to the lack of reliable data for assessing such rate; and to the main factors associated with fetal death and the measures that could be taken to prevent such death. The occurrence of a stillbirth affects the mother, the family, the professionals responsible, the community, and the society. It is a heavy burden for the affected families, and psychological symptoms often persist long after the death of the babies. The authors believe that stigmas and taboos exacerbate the trauma for the families and that fatalism undermines the prevention of stillbirths, which in most cases is possible with the improvement of health services.

Keywords: Stillbirths; Parturition; Gestation; Bariatric Surgery

Introduction

According to the ICD-10 (10th revision of the International Statistical Classification of Diseases and Related Health Problems), stillbirths refer to fetuses with a birth weight of 500 g or more, a gestational age of 22 weeks or older, or a craniocaudal length of 25 cm. For international comparison, the WHO (World Health Organization) recommends the definition of stillbirth as fetal loss in a pregnancy of over 20 weeks or, if the age is not known, a birth weight greater than 500 g, which corresponds to 22 weeks gestational age in a normal gestation [1]. These differences in definition make investigations and comparative studies difficult. The time of intrauterine death is not always known; thus, the presence of maceration is an important marker, implying that death occurred more than 12 hours before parturition.

An estimated two million to six million stillbirths occur annually, 98% of which take place in underdeveloped and developing countries; 75% of cases occur in Africa and Asia [2]. In 2015, the worldwide estimate was 18.4 stillbirths per 1,000 live births, compared with 24.7 per 1000 in 2000. In developed countries, the rate is lower, from two to seven stillbirths per 1000 live births [3]; it can be as low as three per 1000 in some developed countries or as high as 45 in 1000 in developing countries.

Intrauterine fetal death occurs 10 times more often than sudden infant death; however, it is not given much importance. The most common cause of perinatal death is congenital malformation, accounting for 25-40% of cases. Perinatal death is fetal death that occurs after the 28th week of pregnancy until the first week of life. Live birth occurs when the fetus born presents some evidence of life, such as a heartbeat, an umbilical cord pulse, and breathing signals. Autopsies add significant data in 44.7% of cases of stillbirth and may give clues to future risks in pregnancies [4]. Until the ninth week of pregnancy, it is considered embryo. Fetal death is considered early when it occurs before 22 weeks of gestation, intermediate when it occurs from 22-27 weeks of gestation, and late when it occurs after the 28th week of pregnancy.

The literature on stillbirths is limited compared with other issues, such as premature birth, low birth weight, and birth defects. Besides underreporting, uncertainties about the quality of the data make it difficult to characterize and propose improvements. One of the oldest research projects on this subject is the Wisconsin Stillbirth Service Project established in 1983, which analyzes information on stillbirths. Duke, et al., considered intrauterine fetal death as referring to fetuses with 20 or more weeks of gestation and weighing over 350 g [5].

The infant mortality rate is important in: (a) indicating the health of the population and comparing health systems, (b) reporting on the development of public health policies, (c) reporting risk factors, (d) evaluating the programs being developed, and (e) identifying emerging risk factors. During the period 1995-2000, there were 5013 deaths of infants and 5311 fetal deaths out of 649,252 live births (8.95 and 8.18 per 1000 respectively). The relatively high rates of fetal death in the United States have been mostly attributed to premature birth [6].

Each year, an estimated 13 million babies are born before 37 weeks of pregnancy. The rates are highest in the developing world, in which such preterm birth is a major cause of neonatal death (27%). Although the under-five child mortality is improving in many countries, the neonatal mortality remains worrying, accounting for over 42% of deaths under five. Stillbirths, despite having high incidence, are also neglected. One third of all births occur in homes without hospital care. In southern Brazil, mortality in preterm infants is mainly due to respiratory infections, diarrhea, and other infections. Some causes are directly related to the immaturity of the fetus, such as hyaline membrane disease and oxygen-induced retinopathy. Others are associated with intracranial hemorrhage and chronic pulmonary disease [7].

Because nearly half of these births occur at home, stillbirths are understated and underreported. The available data indicate that prolonged labors and various infections without proper treatment are the main causes of stillbirths in developing countries, accounting for 98% of the estimated three million cases annually. These causes include maternal infection, fetal asphyxia, trauma, congenital abnormalities, and fetal-maternal bleeding [8].

In 2014, the World Health Assembly endorsed the target of 12 or fewer stillbirths per 1000 births in every country by 2030. By 2015, 94 countries had already achieved these levels [7].
The aim of the present study was to analyze cases of stillbirth examined in an Institute of Forensic Medicine of the Federal District (IML-DF), Brazil.

**Methods**

This is a retrospective, observational, cross-sectional study that analyzed cases of stillbirth referred to the IML-DF, Brazil, during the period January 2012 to December 2014. The autopsy included the anthropometric profile, external and internal examinations, and histopathologic examination of the viscera and placenta, when the latter was sent with the body. The data extracted from cadaveric reports were gestational age, sex, cause of death, presence of placenta, histopathologic examination of the placenta, and stillbirth and clinical history. The causes were classified as fetal, placental, maternal, and undetermined. The study was approved by the Ethics Committee of the IML-DF.

**Results**

The Institute of Forensic Medicine received 38 cases of stillbirth for examination from public and/or private hospitals over a period of three years (2012 - 2014). Of the 38 stillbirths, 21 were male and 17 were female; the mean gestational age was 32.94 ± 6.38 weeks (Figure 1). In 18 cases, the placenta was sent with the body and could be analyzed. The causes of death were classified as placental, fetal, maternal, and undetermined. The main cause of death was by maternal problems (36.8%), followed by placental disorders (31.5%) and fetal anomalies (7.8%). Undetermined causes accounted for 23.6%, according to the table (Table 1). The average weight was 2,292.65 ± 1130.71 g; in one case, the birth weight was not determined (Figure 2).

**Discussion**

In its first series on the subject, The Lancet (2011) described stillbirths as one of the most shameful and neglected areas of public health. Parents develop serious psychological problems after the loss of a baby. This is an area in which the majority of gynecologists and midwives did not receive training; the 31% who were trained said the training was inadequate. In 2009, Cochrane published a systematic review to support the parents and family after a perinatal death [9].

We analyzed 38 cases of stillbirths referred to the Institute of Forensic Medicine of the Federal District (IML-DF) over a period of three years. The IML-DF doesn’t centralize the analysis of all stillbirths that occur in the Federal District; perhaps many other cases may have occurred without having been referred to the Institute. Therefore, the present study aimed to analyze only those cases sent to the Institute and in which autopsies were carried out.

Of the 38 cases analyzed, 8% had a gestational age of 22 weeks.

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**Figure 1:** Number of cases and gestational age.

**Table 1:** Number of cases and causes of stillbirths.
or less, 21% had 23-27 weeks of gestation, and the majority (71%) had 28 or more weeks of gestation; 53% weighed more than 2500 g. In their research in Brazil, Barber, et al. reported that an estimated 30% of fetal deaths occur in children weighing over 2500 g. In studies that included data on birth weight, the percentage of stillbirths weighing over 2500 g ranged from 24 to 40%. In the cases reported by Duke, et al. the gestational age was 24-33 weeks, and the weight was between 640 and 1900g [3-5].

In the present study, the leading causes of fetal death were of maternal origin (14 of 38 cases), followed by placental (12 of 38), undetermined (9 of 38), and fetal causes (3 of 38). The most frequent causes were hypertensive disorders during pregnancy (5 cases), followed by abdominal trauma (4) and placenta previa (4). Uroos, et al. in a study of 14 cases over a period of five years, found that placental causes were the most frequent cause of fetal death (49.57%), followed by fetal (35.72%) and maternal causes (21.42%); more specifically, congenital anomalies were the most common cause (28.6%). Among the fetal causes were chromosomal abnormalities, birth defects, hydrops, and infection. The placental causes included placenta previa, bleeding, umbilical cord accidents, placental insufficiency, asphyxia, intermellar transfusion, and chorioamnionitis. Among the maternal causes, the main ones were hypertension, diabetes, trauma, difficult deliveries, sepsis, acidosis, hypoxia, uterine rupture, and drug use [10].

The global rate of stillbirths in 2105 was 18.4 per 1000 live births, compared with 24.7 per 1000 in 2000. Although the rate has decreased, the reduction is less than that in neonatal and maternal mortality. Most of the 2.6 million stillbirths yearly take place in underdeveloped or developing countries; 75% of cases occur in Africa and Asia. About 60% of stillbirths happen in rural areas, and more than half in areas of conflict, affecting people with less access to health care. Half of the cases (1.3 million yearly) take place during labor. The deaths occur in babies who, theoretically, are expected to have all the necessary conditions to survive, usually with adequate gestational age [11-12].

The belief that many fetal deaths are inevitable due to congenital anomalies is false because death occurs in only 7.4% of stillbirths that take place after 28 weeks of gestation. The main risk factors are known but looked down on, including maternal age of over 35 years, maternal infection, no reported illnesses, lifestyle, malnutrition, fetal growth retardation, premature delivery, and post-term pregnancy. In developed countries, 90% of fetal deaths occur in the antepartum period and are often associated with preventable factors, such as obesity and smoking [11-12].

Regarding smoking, the good news is that the prevalence of smoking during pregnancy has decreased in many countries; for example, in Sweden, the percentage went down from 31% in 1983 to 7% in 2008 [13]. However, if decreasing the smoking habit is hard, decreasing overweight and obesity is even more difficult. Overweight is more common in women with less schooling but is increasing in all social levels. In the United States, one in three young women is obese. Bariatric surgery may be an option to reduce weight and to improve maternal and fetal survival rates [14-15].

A previous study aimed at comparing the use of illicit drugs and smoking in pregnancies with or without stillbirths analyzed 663 stillbirths. Analysis of the cord was carried out in 63% of the cases, and the most common drug identified was cannabis. This substance has been associated with an increased risk of stillbirth. Both smoking and cotinine level have also been linked to such increased risk [16].

Pinar, et al. identified the cause of death in 57.9% of the cases in their study through placental analysis and autopsy. Placental abnormalities, membranes and cord constituting 25-35% of the causes of death. Placental abnormalities were represented by avascular villi, with fibrous stroma and vessel thrombosis. Infections are common in stillbirths with less than 30 weeks of gestation, whereas hypertensive diseases and diabetes are the two main maternal causes of stillbirth. In the present work, trauma was found to be a major maternal cause of fetal death [17].

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Pinar, et al. compared the placental lesions in stillbirths with those in control cases. They found that single umbilical artery was present in 7.7% of stillbirths and 1.1% of live births, terminal villous immaturity in 10.3% of stillbirths and 2.3% of live births, chorioamnionitis in 30.4% of stillbirths and 12% of live births, degenerative changes in the chorionic plate in 55.7% of stillbirths and 0.5% of live births, retroplacentral bruising in 23.8% of stillbirths and 4.2% of live births, and vascular thrombi in 23% of stillbirths and 7% of live births [18].

Among stillbirths, inflammation and retroplacental hematoma were more common in placentas of premature births, whereas thrombotic lesions were more common in later pregnancies. It is important to note that all the placental lesions found in stillbirths...
can also be found in live births but in smaller proportions. There is no placental change exclusively found in stillbirths.

Roescher, et al. (2014), did a systematic review of placental pathology in the English literature from 1995 - 2013. They found that placental lesions consistent with decreased vascular perfusion were the most important. The main placental problems were ascending infection and thrombotic vasculopathy. In 30% of cases of stillbirths, the cause was unknown. The main contributor to fetal death (34-38% of cases) was impaired maternal vascular perfusion [19].

In our study, difficulties in labor, due to cephalopelvic disproportion or associated with malnutrition, was one of the most important causes of stillbirth. Death can also result from asphyxia, trauma, or infection. In developing countries, the lack of hospital care contributes to many of the causes of stillbirth. Other risk factors in these countries include advanced maternal age, low socioeconomic level, malnutrition, and previous history of stillbirth. About 50% of intrapartum stillbirths were due to obstetric complications. In half of the cases, the cause could not be determined. Most fetal deaths can be prevented by improved access to qualified health services. Global estimates suggest that about one third of stillbirths occur during the intrapartum period. However, a prospective study in five countries showed that only 17% were macerated, suggesting a higher proportion of intrapartum deaths [20].

Regarding time of death, the majority of stillbirths (two of three) occur antenatally, as evidenced by the appearance of maceration on the fetuses; the other cases are associated with labor complications. Depending on the access to and quality of obstetric care and the antenatal prevalence of risk factors, the proportion of stillbirths may vary. Habits such as smoking, exposure to other toxic substances, lack of nutrition to the fetus, genetic abnormalities, and maternal infection are also among the defined factors. In a literature review, Yakoob, et al., suggested measures that could improve these indices, such as prevention of genital mutilation, longer intervals between pregnancies, reduced exposure to pollution, cessation of smoking and exposure to tobacco, and supplementation of folic acid, vitamin A, micronutrients, and magnesium [21].

In the United States, death certificates are filled out by clinical assistants without further investigation. Since 1950, there has been a decline in stillbirth rates but not to the extent of neonatal deaths. One of the largest analyses of causes of fetal death was done in Canada and included 709 stillbirths in 88,651 live births, 97% of which underwent autopsy [22]. Since the introduction of HR plasma lysins of immune response, there has been a 95% reduction in stillbirth rates. After intrapartum monitoring, the rate of stillbirths due to asphyxia has decreased by 95%.

In the present work, the mean birth weight was 2292.65 ± 1130.71 g, with 47% of fetuses weighing less than 2500 g. Those that are small for their gestational age (below percentile 2.4) showed an incidence of 46.8 stillbirths per 1000 live births, whereas those with an adequate weight for their age showed a rate of four per 1000. The identification and appropriate treatment of growth retardation remains a significant opportunity for prevention. Between 24 and 27 weeks of gestation, the most common causes of stillbirth were related to infection (19%), placental abruption (14%), and severe abnormalities (14%); 21% were due to undetermined causes [22].

Multiple factors may act directly or indirectly on the fetus in the mother. Infection accounts for almost half of stillbirths in developing countries. Placental infection may stem from the mother or may be direct, resulting in decreased placental flow. Infections with gram-negative organisms, such as *Escherichia coli* or *Klebsiella pneumoniae*, are more common. Syphilis is prevalent in Africa, in which more than 10% of pregnant women are HIV-positive. Many cases occur in malaria-endemic areas, causing placental damage. Chagas disease, which is common in South America, can infect the fetus and placenta [23].

In our study, the rate of infection that can be detected was low, two in 38 cases (5.2%). Despite efforts to decrease the risk of infection by streptococcus, particularly type B, there has been little reduction in the risk of stillbirth. Among some pathogens that can also cause fetal death are parvovirus 19, cytomegalovirus, toxoplasma, and listeria.

Infection can cause fetal death by several mechanisms, including direct infection, placental damage, and severe maternal illness. Infections can be due to viruses, bacteria, and protozoa. In developed countries, 10-25% of stillbirths are caused by infection, whereas in developing countries, the role of infection is much higher. In developed countries, ascending bacterial infection, before or after membrane rupture, with organisms such as *E. coli*, streptococcus type B, and ureaplasma urealyticum, is the most common. The two most important viral causes are parvovirus and Coxsackie virus; toxoplasmosis, listeria infection, and leptospirosis have also been implicated in the etiology.

Infection is more associated with low gestational age (20-28 weeks). The identification of organisms in the fetus or the placenta does not prove causality. Maternal infection can cause fetal death, without fetus infection, only causing systemic maternal disease [23].

In cases of spirochete infection, the bacteria (*Treponema pallidum*) cross the placenta and infect the fetus (above 14 weeks of gestation); in 45% of cases, fetal death occurs. In malaria, especially falciparum malaria, when the parasite infects the placenta, placental insufficiency results from the accumulation of lymphocytes and macrophages, the thickening of the trophoblastic membrane, and the increase in various inflammatory cytokines, all of which contribute to the decrease in placental flow. The main virus implicated in fetal death is parvovirus, which is responsible for a rash (infectious erythema) in children; the virus crosses the placenta and attacks the erythropoietic system, causing fetal anemia, hydrops, and death.

Bacterial infection results in fetal death from pneumonitis. *Streptococcus* type B, *E. coli*, and *Enterococcus* are the main organisms found in the internal organs during autopsy. When streptococcus bacteria reach the uterus, they undergo rapid replication in amniotic fluid infection with little involvement of the membranes. Two other pathogens should be mentioned: *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Bacteria also reach the fetus through the placenta. In such cases, the placenta presents evidence of infection, including inflammatory response, microabscess, and stroke. The organisms usually enter the fetus through the umbilical vein; thus, the liver is the organ most often infected [23].

It was not possible to verify the incidence of risk factors in our study. The identification of risk factors is important toward preventing fetal deaths and proposing public health policies to reduce mortality rates. Among the risk factors that have been previously identified and discussed are socioeconomic factors and race (black women); undetermined causes have been found to increase with advancing gestational age. In general, black women have low educational levels and poor living conditions, and received inadequate prenatal care. Statistically, women over 35 years have an increased incidence of premature and low-weight children, as well as a higher rate of congenital anomalies in their children. Obesity is another important factor because it is associated with fetal macrosomia and perinatal mortality. Obese pregnant women
are more prone to diabetes, preeclampsia, and smoking, and have a lower ability to recognize decreased fetal movements. Dyspnea in sleep is more common in these women and may lead to episodes of oxygen desaturation [1].

Baqui, et al. reported their experience with virtual autopsies. In their study during the period 2003-2005, they found 1,748 stillbirths out of a total of 48,192 births, a rate of 3.6 per 1000 births; virtual autopsy was done in 90.6% of the cases. Eighty percent of stillbirths took place in the home, and most occurred vaginally without any assistance. Among the stillbirths, 62% were antenatal, and 38% were intrapartum; 13% of mothers reported that the fetus was macerated or had previously stopped moving. Among the cases of antepartum death, about 29% had symptoms suggestive of maternal disease, including infection (19%), hypertension (9%), and severe anemia (2%). The main cause of death was hypoxia due to abnormal presentation. Despite its limitations, verbal autopsy is the only method available in developing areas without access to medical care [20].

Aggarwal, et al. agreed with the use of verbal autopsies, particularly in developing countries where the available data, which are based on hospital information, suggest that difficult or prolonged labor, preeclampsia, and infection account for the majority of stillbirths. These data, however, are not reliable because most stillbirths occur in homes, and many hospitals are not adequately equipped to investigate the causes of fetal death [24].

Knowing the risk factors and given the possibility of preventing the majority of fetal deaths, several authors have suggested measures to decrease the fetal mortality rate. Menezes, et al. carried out a systematic review of 16 antenatal interventions with the potential to prevent stillbirths. Various interventions have shown clear evidence of success, such as aspirin therapy for certain maternal indications, treatment and screening for syphilis, malaria prevention, treatment of intrahepatic cholestasis, and maternal antihypertensive treatment [25].

The use of antihypertensive drugs is important because high blood pressure, which causes restriction of placental flow or placental abruption, is related to prematurity and fetal growth retardation. Calcium supplementation prevents hypertension. Another measure suggested is the use of antiplatelet agents for hypoxic placental release in maternal circulation factors that activate platelets and coagulation systems. Preeclampsia is characterized by an insufficient level of prostacyclin (vasodilator) and excessive production of thromboxane, a vasoconstrictor that stimulates platelet aggregation. The use of antiplatelet agents, on the other hand, increases the risk of fetal and maternal bleeding. Heparin and other agents can also be used prophylactically because pregnancy and puerperium are associated with an increased risk of thromboembolism. One concern is that warfarin is known as a teratogenic agent [25].

The time of birth, birth, and first years of life are the most vulnerable periods for mothers and children. Michałów, et al. assessed the costs and gains that could result from implementing measures to prevent fetal death in South Africa, which they believe could decrease the number of stillbirths by 30%, from 17.6 per 1000 live births in 2013 to 12.4 per 1000 live births by 2030. About 55 stillbirths occur daily in South Africa, even with almost 90% of births taking place in hospitals. Almost two thirds occur antepartum, and 50% are concerned as undetermined cause death [26].

Thirteen measures to prevent the incidence of stillbirths have been proposed: syphilis detection and treatment; prevention, diagnosis, and control of hypertension; treatment of diabetes; treatment of preeclampsia with magnesium sulfate; detection and treatment of growth retardation; better obstetric care; better prenatal care; early detection of HIV; immunization against tetanus; use of antibiotics in cases of premature rupture of membranes; and use of corticosteroids for preterm birth [26].

Conclusion
Our series revealed a profile of stillbirth in a developing country like Brazil. Most of cases showed that maternal and placental problems were mainly responsible for the incidence of stillbirth, factors that could be avoided since we had better care for pregnant women.

Stillbirths remain one of the most common adverse effects of pregnancy but is also among the least studied. Many cases remain undocumented and have not been included in the health index. Negative psychological symptoms are common in parents of stillborns, often persisting for years after the death of the baby. An estimated 4.1 million women are living with depression associated with stillbirth. The inclusion of stillbirth in the integrated health programs to be implemented, that can be valued and known, since they can be largely prevented. The series published by The Lancet (2016) draws attention to three points to determine if stillbirths are effectively integrated into international health standards for women and children. First, has stillbirth been included in relevant summaries of the burden of maternal, neonatal, and child mortality? Second, is high-quality antenatal and intrapartum care included in specific interventions to prevent stillbirths? Finally, are stillbirths monitored through the use of a target, an outcome indicator, or both? [27].

References


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