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REVIEW ARTICLE

Epidemiology and Prevention of Fetal Death and Stillbirth

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ABSTRACT

In high-income countries, the stillbirth rate did not change during the last decades. For prevention of stillbirth we need an international consens about risk factors, causes and classification of stillbirth, national fetal registries and standadized protocols for stillbirth evaluation. The knowledge from these data may lead to further prevention strategies.

Keywords: Fetal autopsy, Fetal death, Placental histology, Stillbirth.

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DEFINITION OF STILLBIRTH

Internationally, there are many different definitions to define a stillbirth, most of these differences relate to the gestational age of the pregnancy or the fetal weight. According to the World Health Organization,[1] a stillbirth is "... a baby born with no signs of life at or after 28 weeks' gestation" while according to the Centers for Disease Control a stillbirth is "... the death of a baby before or during delivery."[2]

Some statistics of stillbirths exclude newborns with congenital anomalies or termination of pregnancy. These differences may have an influence at the precise rate of stillbirth, but the global trend will persist.

INCIDENCE OF STILLBIRTH

Worldwide, on average, six stillbirths occur each minute or nearly 3 million each year.[3] The stillbirth rate has declined by 14% from 22.1 per 1,000 births in 1995 to 18.9 stillbirths per 1,000 births in 2009, though there is a dearth of reliable data in regions where most stillbirths occur.[4] In high-income countries the stillbirth rate has remained constant for the past three decades, ranging from 3 to 5.3 per 1,000 births.[5]

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RISK FACTORS FOR STILLBIRTH

A systematic review and analysis for identifying major risk factors was suggested by Flenady et al.[6] The more significant risk factors included maternal overweight and obesity, maternal smoking, small size for gestational age, placental abruption, preexisting maternal diabetes and hypertension, and primiparity.

Villamor and Cnattingius[7] from Sweden reported the increasing risk with weight gain between pregnancies. Overweight and obesity increase the risk of diabetes type 2 and gestational diabetes, which increased the risk for stillbirths, too. The number of women with delayed motherhood is rising, specifically in high-income countries, which is leading to an increase of primiparous women older than 35 years. Stephansson et al[8] found an odds ratio of 3.6 for stillborn risk in older primiparous women (>31 years). Waldenström et al[9] described that maternal age is an independent risk factor for stillbirth in nulliparopus women. Pregnant women without or late antenatal care showed high odds ratios for stillbirth. Globally, low education level (8 years or fewer) and other low socioeconomic status measured by employment, marital status, and income increase the odds ratio for stillbirth clearly.

CAUSE OF STILLBIRTH

The topic of stillbirths especially in low-income countries (according to the World Bank countries classification) has received very little research or attention. Despite the large number of stillbirths worldwide, there is no standard international classification system for the cause of a stillbirth. Almost half of the deliveries in many developing countries occur at home, and underreporting of stillbirths is a significant problem. Reliable data about rates and causes are unavailable in many areas of the world.[10] Higher and lower income countries have different stillbirth rates and causes, which often require different preventive strategies.[11]

The classification of fetal deaths is further complicated by the multiplicity of factors and pathophysiological processes regarding mother, fetus, and placenta. There are many classification systems published in the literature.[12]

Better than the pathoanatomical and clinical mixed classification system may be the two-step classification: (1) The indirect causes of fetal death as the result of autopsy and placental histology; (2) The risk factors from clinical reasons.[13]

In order to appropriately address whether the fetal death was caused spontaneously or as part of an induced termination of pregnancy – e.g., 55% of all fetal deaths in 2010 in Canada were part of an induced termination of pregnancy[14] – fetal death registries are essential, partially to establish effective prevention strategies.

Prolonged and obstructed labor, preeclampsia, and various infections, all without adequate treatment, appear to account for the majority of stillbirths in developing countries.[10]

According to the Stillbirth Collaborative Research Network Writing Group, the majority of stillbirths had a probable or possible cause after a systemic evaluation, with obstetric conditions and placental anomalies among the most common causes,[15] while in a Scandinavian study, two-thirds of all stillbirths were caused or were associated with placental pathology.[16] Michalski et al[17] studied nearly 1,500 stillbirths. Autopsy findings identified the cause of death in 46% of cases and gave new information in 51%, which changed the estimated recurrence risk in 40% of cases. Hübner et al[18] published a retrospective 8.5-year study of eight hospitals with clinical reports, data collection, interdisciplinary communication, and postmortem examination in the area of Bonn/Germany in which 52% were of a certain or uncertain cause of death.

EVALUATION OF STILLBIRTH

Optimally, all stillbirths should have a thorough evaluation done to confirm not only the cause of the stillbirth but also to recognize contributing factors. Several organizations have developed standardized protocols for stillbirth evaluation.[11] Therefore, timely autopsy and placental histopathology performed by an experienced perinatal pathologist are crucial steps. Unfortunately, in low-income countries, access to perinatal pathologists is limited, and even in high-income countries they are not always available. The combined approach (clinical records including maternal laboratory evaluation,[19] fetal autopsy, placental histology) will lead to a clarification of the cause in the majority of stillbirths.[15,20] Inadequate postmortem examination will determine unexplained fetal deaths.

In cases when the parents do not accept the autopsy despite of compassionate counseling, minimally invasive approaches like radiological imaging, skeletal survey, or postmortem magnetic resonance imaging and blood sample collecting for cytogenetic are—partially—alternative methods of conventional autopsy. Nevertheless, appropriate counseling of the parents improve the autopsy rate.

PLACENTAL FINDINGS

Pinar et al[21] compared placental lesions for 518 stillbirth cases and 1,200 live birth controls in a population-based study. They found significantly higher rates in stillbirth cases with single umbilical artery, velamentous cord insertion, diffuse terminal villous immaturity, inflammation like chorioamnionitis, vascular degenerative changes in chorionic plate, retroplacental hematoma, intraparenchymal thrombi, parenchymal infarction, fibrin deposition, fetal vascular thrombi, avascular villi, and placental hydrops.

PREVENTION STRATEGY

Searches in international peer-reviewed papers about stillbirth and some retrospective data collection in different areas of high-income countries showed the necessity of a standardized and complete postmortem procedure for development of effective prevention strategy.[12]

The raising of awareness and implementation of effective interventions for modifiable risk factors, such as overweight, obesity, maternal age, and smoking, are priorities for stillbirth prevention in high-income countries.[7] Considering the evidence of obesity as one of the leading risk factors for stillbirth, strategies are needed to educate women in childbearing age about optimizing normal body mass index. Moreover, strategies against smoking and alcohol drinking, and promotion of smoking and alcohol cessation in pregnancy must be more effective.

Stillbirths can be further lowered by preconceptional treatments of medical disorders like diabetes, thyroid disorders, and hypertension. Therefore, preconceptional medical counseling is important for all women in childbearing age.

An advanced maternal age over 35 years especially in primiparous women contributes to the stillbirth rate of high-income countries. Strategies to decrease the mean maternal age are difficult to realize in our communities, but there are some policies for women with the decision for postponed motherhood.[22]

CONCLUSION

In low-income countries, better access to appropriate obstetric care, particularly during labor and delivery, and better screening and treatment of syphilis can reduce stillbirth rates dramatically, while in high-income countries, effective interventions for modifiable risk factors, such as overweight, obesity, maternal age, and smoking, are priorities for stillbirth prevention.

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