

Stillbirth

Understanding and Management

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12 Classification of stillbirth: A global approach

Jason Gardosi and Robert Pattinson

Stillbirth is a devastating event not only for the baby, but also for the mother and father, the wider family, the health service, and the community as a whole. However, the significance of the loss and its effect on the grieving mother or parents is often underrated. There is increasing evidence that many deaths are potentially preventable, and stillbirth rates are starting to be recognized as an important indicator of the quality of care.(1) A suitable classification system is central to any effort to reduce its incidence.

Causes and Conditions

There are two principal purposes for classification systems, and these are not mutually exclusive. The first is to improve our understanding of the causes, and the events which have led to the death. A recent NIH/NICHHD sponsored expert workshop (2) agreed that a valuable classification system for research would identify the pathophysiological entity initiating the chain of events that irreversibly led to death, based on pathologic, clinical, and diagnostic data. The criteria to be used to categorize a particular condition as a *cause* of stillbirth should consider the following principles:

1. There is epidemiologic data demonstrating an excess of stillbirth associated with the condition.
2. There is biologic plausibility that the condition causes stillbirth.
3. The condition is either rarely seen in association with liveborns or when seen in liveborns results in a significant increase in neonatal death.
4. A dose–response relationship exists so that the greater the “dose” of the condition, the greater the likelihood of fetal death.
5. The condition is associated with evidence of fetal compromise.
6. The stillbirth would likely not have occurred if that condition had not been present, that is, lethality.

Another approach is more pragmatic, suggesting that while often a cause cannot be found, the stillbirth can still be described in terms of what happened, and that this is immediately relevant to highlight issues for clinicians and planners or commissioners of the health service, and to seek to make improvements based on the information available.

While much of the research on perinatal loss has been performed in developed countries, an essential perspective in any discussion of classification systems is its international applicability. Over 90% of the estimated 3.2 million stillbirths per year occur in

underdeveloped countries (3), and classification systems need to take such inequality in the “burden” of stillbirths into account. It is this second need for classification systems which is the main focus of this chapter.

The following discussion will first examine the classifications in developed countries and then the need in developing countries, before summarizing recent efforts to move toward a system which is globally applicable.

Classifications in developed countries

Classifications need to reflect the main causes and conditions of fetal demise. In “developed” countries, these comprise congenital anomalies, including chromosomal and structural conditions such as neural tube defects; maternal conditions such as hypertensive diseases including preeclampsia, diabetes, and other endocrinological disorders; systemic lupus erythematosus, thrombophilias, cholestasis of pregnancy; and multiple pregnancy related conditions including twin-twin transfusion syndrome. Intrapartum-related deaths, while an important category, are much fewer than in developing countries (see the subsequent section). Infections may include maternal transmission (e.g., parvovirus 19, cytomegalovirus, and primary herpes simplex) but are more likely acquired through the ascending route, such as Group B *Streptococcus*.

However until recently, the majority of stillbirths have been classified as “unexplained”.(4) In the United Kingdom, the preponderance of an unspecified or unexplained category has occurred despite three classification methods: a) the pathophysiological classification by Wigglesworth (5); b) the fetal and neonatal classification (6) based on a system first described by Bound et al. in 1954 (7) and applied in the 1958 British Mortality Survey (8); and c) the revised Aberdeen “Obstetric” classification (9), which was based on a method first described by Baird and Thomson in 1954.(10) Many other classification systems have been published in recent years—a fact which in itself illustrates that there is no single universally accepted system. Gordijn et al. (11) reviewed 35 classifications systems and found substantial variation in definitions and approaches.

The usefulness of a classification system which results in most cases being “unexplained” or “unclassified” is questionable.(12) While it might be a prompt for further research, in everyday care such terms are often taken as being synonymous with “unavoidable,” which has connotations for all parties concerned: the parents who are seeking explanations and are trying to come to terms with the loss; the clinicians who are seeking to advise the mother on the implications and plans for future pregnancies; the health care institutions which need to review

the service they are providing; and the planners and commissioners who are seeking to improve the service. Perhaps related to this is the lack of advancement in avoidance of stillbirths: Contrary to the consistent gradual reduction of neonatal and infant mortality, the United Kingdom has seen very little change in stillbirth rates in recent years (13), and similar observations have been made elsewhere.

One recurring obstacle to identify and address the problem relates to the fact that classification systems tend to seek to establish a “cause” of death. However very often, the causes have not been sufficiently investigated, or the investigations are not available. Postmortem rates, for example, vary substantially between countries and over time; in some health systems, they are not freely available, and in some communities they are not accepted on cultural or religious grounds. Even full investigation may not affect the proportion of cases considered “unexplained” because of the rigidity of the classification system. For example, using Wigglesworth, a similar proportion of cases with (69%) and without a postmortem (60%) were categorized as “unexplained” in a UK cohort of stillbirths.(14)

An alternative approach is to describe “what” has happened, using a classification which focuses on clinical conditions, and results in messages which are clinically relevant. This principle has been proposed with the “relevant condition at death” (ReCoDe) classification.(15) The method was applied to a cohort of stillbirths which occurred in the West Midlands from 1995 to 2005, and was found to reduce the size of the “unexplained” category to 16%. This method allowed conditions to be included which described “what” happened, without claiming any causal explanation. The most important of these new categories was fetal growth restriction, defined retrospectively by customized centiles which adjust the normal limits of birthweight-for-gestation according to maternal constitutional characteristics. On its own, it accounted for over 40% of stillbirths, and if congenital anomalies were excluded, over half of the remaining stillbirths were preceded by intrauterine growth restriction (IUGR). While growth restriction was not a “cause” for fetal demise, it reflected the clinical manifestation of underlying conditions such as placental disease.

Similar findings are being reported in audits in England (16), Ireland (17), and Norway .(18) Froen et al. studied a Norwegian cohort of stillbirths which were considered “unexplained” even after undergoing comprehensive investigations including post-mortems. Over half of these stillbirths were found to have fetal growth restriction.(18)

Such findings are important information for the mother, her clinicians, and health service planners. In the West Midlands, they have led to a firm maternity care focus on the need to improve antenatal recognition of fetal growth restriction, with evidence of improvements in the rate of detection, and serve as an example of how better classification of stillbirth can lead to service enhancements. The findings are also pertinent to researchers and allow them to concentrate efforts on understanding the causes and developing early indicators and/or treatments for placental insufficiency.

To take further the concept of distinguishing condition (what) and cause (why), a three-tier perinatal classification of “when,” “what,” and “why” has been proposed.(11) First, the “when” establishes the timing of the death—antenatal, intrapartum, and neonatal as well as the gestational age of the fetus or neonate, as in the Nordic/Baltic classification.(19) “What” describes the relevant conditions as in ReCoDe (15), and the “why” seeks to establish in more detail the underlying cause, as applied in the Tulip classification.(20) Tulip focuses in particular on the various placental and placental bed conditions associated with perinatal deaths.(21)

Classification for developing countries

The needs of low and middle income countries to reduce adverse perinatal outcomes are wide ranging. At one end, there are large centers of excellence where clinicians deal with conditions which their colleagues in richer countries know only from textbooks. At the same time, many rural communities are devoid of maternity care, many of the births are at home rather than in facilities, and there is little if any record of perinatal outcome. Health care workers seeking to collect information often have to rely on relatives and neighbors to obtain a history of events (“verbal autopsy”).

A key role for classification systems in this setting is to ensure the identification of *when* the death has occurred. The Wigglesworth classification provides a method in which this can be highlighted. Furthermore, the Aberdeen classification (10), modified for use in developing countries (22), is able to focus on underlying obstetric events.

Deaths during labor are much more common (23, 24), because of poor access to facilities or because of insufficient operative delivery services. Thus, obstructed or prolonged labor and associated asphyxia are important categories. Prolonged labor due to fetopelvic disproportion from contracted pelvises associated with childhood malnutrition is an important cause of stillbirth in developing countries. However, fetuses do not die from the labor itself, but from asphyxia, trauma and infection that often accompany prolonged labor.(25) In developed countries, cesarean sections reduce the impact of these complications. It has been estimated that cesarean section rates of about 5% are needed to reduce the morbidity and mortality associated with prolonged labors, but often the cesarean section rate is < 1%.(26) A related cause of stillbirth in developing countries is fetal malposition. In developed countries, these fetuses are generally delivered by cesarean section to prevent the complications of prolonged labor, asphyxia, and birth trauma. However, when cesarean sections are unavailable, mortality from these complications is high. Similarly, twin pregnancies are often complicated by malpositions, prolonged labor, and high fetal mortality from the same causes.

Another important function for the classification, in particular in developing countries is to highlight the contributing role of maternal conditions arising during pregnancy, for example due to preeclampsia/eclampsia. In geographic areas

where blood pressure and urine protein screening are not routine, and where induction of labor or cesarean sections are not accessible, fetuses frequently die secondary to hypoxia associated with maternal preeclampsia or eclamptic seizures.

Often the conditions exist before the pregnancy, such as poor nutritional status, malaria, or sickle cell disease. The baby may have congenitally acquired infections such as syphilis, TB, and HIV. In developing countries, estimates suggest that infection contributes to nearly half of the stillbirths.⁽²⁷⁾ Maternal infection may result in systemic illness, high maternal fever, or respiratory distress leading to fetal death without the organisms having been transmitted; the placenta may be directly infected without spread of the organisms to the fetus, resulting in placental failure and reduced blood flow; or the fetus may be infected resulting in damage to its vital organs. Each of these mechanisms is more commonly associated with the perinatal infections present in developing countries. Acquired or ascending infections, usually associated with chorioamnionitis, can include Gram negative organisms such as *Klebsiella pneumoniae* or *Escherichia coli* as the most common causal agents.⁽²⁵⁾

Principles for an international classification

The large numbers of classification systems in existence are the result of the lack of any one system which can address the needs of different environments and settings. It is tempting to suggest that classification systems need to be home grown and customized to the needs of a particular country and a particular level of investigations and care. However, this would prevent meaningful international comparisons. Recent efforts have therefore focused on the development of a method which allows such comparisons between, as well as within, different settings, including low, middle, and high income countries. This will allow benchmarking and comparisons, and identify systems failures, trends, and modifiable factors. Importantly, this approach will recognize the need to focus on the areas where most deaths occur.

The following main principles have emerged:

1. The classification system needs to include stillbirths as well as neonatal deaths, and start with the need to establish whether the death has occurred antepartum or intrapartum, or in the early (first week) or late neonatal period.
2. It should result in a table that can be used by all countries for meaningful comparison.
3. Therefore, the classification needs to be multilayered to allow input of the varying levels of available information. It should thus be able to accommodate verbal autopsies, clinical history or diagnosis, as well as laboratory (including autopsy and histology) investigations.
4. Thus the layers of the classification should help determine
 - (a) the *timing* of the death (antenatal, intrapartum, early or late neonatal);
 - (b) a list of mutually exclusive clinical *conditions*; which link into

(c) subcategories representing a third, diagnostic level, establishing where possible, the *causes* and events leading to death.

5. For each case, one principal maternal/obstetric condition and one principal fetal/neonatal condition is to be listed, corresponding broadly to the respective "O" (obstetric) and "P" (perinatal) groupings of the ICD codes. Risk factors (smoking, obesity, etc.) should be recorded separately from the clinical condition.

The maternal conditions will dovetail with the emerging international WHO maternal classification system, and include indirect (preexisting) conditions. The aim is to record all known conditions/clinical entities so as to retain all possible information. For each case, a principal maternal and a principal fetal/neonatal condition is then determined according to hierarchical rules. The manner in which the results are reported will vary according to local priorities (e.g., obstetric hemorrhage, intrapartum asphyxia, or neonatal infection) in different countries or regions.

Work is currently underway to refine the conditions and categories of such an international classification system, and to link it in with the development of the new ICD 11 codes. Ultimately, the proof of principle will lie with the ability to classify and understand perinatal deaths in different environments, considering the different levels of information available.

The link to the mother is hoped to have other advantages other than to identify the maternal causes and conditions leading to fetal compromise. For various reasons, perinatal deaths, and in particular stillbirths, are grossly underreported in many resource-poor countries. They may be low in priority in overstretched and under-resourced health services. Ascertainment will improve with better data on all pregnancies, collected as early as possible during routine antenatal care. Linking efforts to improve maternal health with stillbirth prevention recognizes the interrelatedness of both, as joint priorities for improving maternity services.

CONCLUSION

Classification helps in the understanding of the underlying factors and events leading to perinatal death. It is essential for the establishment of priorities of the health service to identify the gaps and highlight the need for strategies for prevention.

A universally accepted classification will help countries or districts to benchmark and compare their mortality rates and the associated factors or underlying causes. This in turn will aid in the push for the appropriate resources to fill health gaps and to develop equitable services which can recognize and respond to local challenges.

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