COMMENTARY

Analysis of Perinatal Mortality and Its Components: Time for a Change?

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Since the midtwentieth century, stillbirths (late fetal deaths) and early neonatal deaths have often been combined into a single category of “perinatal” deaths. In the past, such a combination was justified by the fact that asphyxia was a common cause of death during labor (intrapartum stillbirth) and shortly after birth and by geographic and temporal differences in classification of livebirths versus stillbirths. In more recent years, however, the etiologic determinants have diverged sharply, with many fewer early neonatal deaths caused by asphyxia and relatively many more caused by congenital anomalies. Moreover, the increasingly common stratification of pregnancy outcome measures by gestational age or birth weight leads to the use of an inappropriate denominator (total livebirths plus stillbirths within each gestational age or birth weight category) for denoting risk for the stillbirth component, because all unborn fetuses (including the majority of those not born within the specified gestational age or birth weight range) are at risk of being stillborn in that range. The authors suggest that, whenever possible, stillbirths and early neonatal deaths should be reported separately, with gestational age-specific risks of stillbirth based on all fetuses at risk, and that antepartum and intrapartum stillbirths be reported separately. Am J Epidemiol 2002;156:493–7.

RATIONAL FOR COMBINING STILLBIRTHS AND EARLY NEONATAL DEATHS

Anyone who has witnessed a large number of deliveries is aware of the occasional difficulty in distinguishing stillborn infants from those liveborn infants who are extremely preterm (near the limit of viability), asphyxiated, or neurologically depressed and who die soon after birth. Because of this difficulty, the World Health Organization developed and promulgated what is currently the universally adopted definition of a livebirth: “...the complete expulsion or extrac-
tion from its mother of a product of conception, irrespective of the duration of pregnancy, which, after such separation, breathes or shows any evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut, or the placenta is attached; each product of such a birth is considered liveborn” (1, p. 129). Despite the widespread acceptance of this definition, its application has varied widely among countries, among geographic regions within countries, and over time even within geographic regions (2). Cultural, economic, and religious factors all play a role in deciding whether a birth is registered as a livebirth or a stillbirth or whether it remains unregistered as either.

In England and Wales, stillbirths first became registrable in 1928. In 1949, they were combined with early neonatal deaths (those occurring during the first week after a livebirth) to form the perinatal mortality rate, which was then 38.1 per 1,000 total births (3). This combination of stillbirths and early neonatal deaths was later adopted internationally in an effort to minimize variations in the classification of livebirths versus stillbirths and thereby permit valid international, regional, and temporal comparisons. At the time, such a combination appeared justified because asphyxia was a major cause of both stillbirths (especially those occurring during labor) and early neonatal deaths (4).

The definition of perinatal mortality has itself varied geographically and temporally, however. Jurisdictions differ in terms of the lower limits of gestational age or birth weight for registering a late fetal death (stillbirth) and thereby distinguishing the event from an early fetal death (also referred to as a miscarriage or spontaneous abortion). Jurisdictions where late fetal deaths are officially registered at 20 or more or 22 or more weeks (or ≥500 g) have clearly witnessed an increase in such registrations in recent years (5, 6). Increasing numbers of livebirths have also been reported at these gestational ages in several recent publications from both Canada (7, 8) and the United States (9). The likely reason for these increases is the improving viability of extremely preterm infants. In Canada, for example, a dramatic fall in mortality for infants born at 25–27 weeks of gestation occurred from 1991 to 1997, from 318 to 219 per 1,000 infants (p < 0.0001 based on χ² test for trend) (Canadian Perinatal Surveillance System, unpublished data).

In other jurisdictions, registration practices differ for stillbirths and livebirths. For example, Sweden continues to restrict registration of stillbirths (late fetal deaths) to those that occur at 28 or more weeks of gestation. Thus, a 26- or 27-week infant born with signs of life should be registered as a livebirth and, if death occurs within the first week, as an early neonatal death. However, the same infant without signs of life would not meet the criteria for late fetal death and would therefore go unregistered. Thus, an “asymmetry” exists between the two components of perinatal death at gestational ages below 28 weeks. This asymmetry may create an incentive to classify an extremely preterm, liveborn infant with early signs of life who dies shortly after birth as stillborn rather than liveborn, thereby avoiding registration entirely and sparing the family, physician, and hospital the emotional and financial burdens of registration, funeral rites, and burial (2).

In other settings, cultural, religious, and economic factors may exert an opposite influence. Some families may prefer to register, name, and bury a stillborn or a liveborn infant near the borderline of viability who later dies as a way of “healing” their loss, and in some jurisdictions, maternity leave benefits may depend on registration.

ETIOLOGIC DIFFERENCES BETWEEN STILLBIRTHS AND EARLY NEONATAL DEATHS

Stillbirths and early neonatal deaths differ substantially with respect to their principal causes. As discussed in the previous section, this may have been less true several decades ago, when many more term infants died of asphyxia during labor or shortly after birth (4). Even today, conditions such as abruptio placentae and fetal growth restriction can cause either stillbirth or early neonatal death. However, in most developed countries at the present time, the etiologic differences are far more striking than the similarities.

Fetuses with congenital anomalies incompatible with fetal growth and development are often aborted early in gestation (first trimester) (10, 11). Other anomalies, however, do not become life threatening until birth. For example, an in utero existence protects fetuses with severe congenital heart defects that lead to physiologic compromise only after birth and the relative shift from pulmonary to systemic blood flow. Similarly, congenital abnormalities of the gastrointestinal tract (e.g., tracheoesophageal fistula) or lungs (e.g., pulmonary hypoplasia) only become life threatening after the enteral nutrition and respiratory function, respectively, required by extraterine life. Unpublished data from the linked birth, stillbirth, and infant death file of the Canadian Perinatal Surveillance System support these physiologic arguments. Among singleton births at 25 weeks or more in Canada in 1991–1997, for example, the risk of stillbirth due to congenital anomalies was only 3.8 per 10,000 total births, whereas the risk of early neonatal death due to congenital anomalies was 9.3 per 10,000 livebirths. The corresponding risks for death due to asphyxia were reversed: 17.1 per 10,000 for stillbirths and 2.9 per 10,000 for early neonatal deaths. Congenital anomalies caused 45.8 percent of early neonatal deaths versus 9.4 percent of stillbirths, while the reverse trend was observed for deaths due to asphyxia: 14.4 percent of early neonatal deaths versus 42.5 percent of stillbirths.

Moreover, etiologic determinants differ widely according to whether the stillbirth occurs antepartum or intrapartum, that is, before or during labor. Antepartum stillbirths often occur with severe maternal, placental, or fetal abnormalities, including umbilical cord complications (12–14), preeclampsia (14, 15), intrauterine growth restriction (12, 13, 16–19), abruptio placentae (14, 20), and infection (21, 22). Maternal smoking, advanced maternal age, grand multiparity, and obesity are also widely recognized determinants of antepartum stillbirth (12–16, 23–25), while one fourth occur without known cause (13, 15).

Intrapartum fetal deaths are usually the result of fetal distress and/or obstructed labor and often reflect poor access to or quality of clinical care during delivery (26). In developed countries, the vast majority (85–90 percent) of stillbirths occur antepartum (12, 26), whereas this proportion is
much lower and the overall stillbirth rate is much higher in
developing countries (16). This is particularly true in settings
where deliveries occur at home and are attended by
untrained traditional birth attendants or without access to
emergency obstetric care or where distances to such care
pose a risk to fetal survival during labor.

PERINATAL MORTALITY “RATE”: PROPORTION
VERSUS HAZARD

Even if the above inconsistencies of definition, registra-
tion, and etiology did not exist, there would be major prob-
lems in the way that perinatal mortality rates are used to
reflect the risk of mortality. Neonatal mortality is a straight-
forward concept; it conditions on a livebirth, and all liveborn
infants are at risk of death. The risk of early neonatal death is
thus denoted as the number of deaths occurring in the first
week of life divided by the number of livebirths. Defining
the risk of stillbirth, however, is a bit trickier. No problem
arises for the overall rate of stillbirths, which, despite the
term rate, is correctly denoted by the proportion of stillbirths
among all births (stillbirths plus livebirths). Once the lower
reporting for limits for gestational age and/or birth weight
are agreed upon and are applied equally for stillbirths and
livebirths, this overall rate of stillbirths accurately reflects
the total proportion of all such births that are stillbirths.

The difficulty develops when the overall stillbirth rate is
stratified by either gestational age or birth weight. For
example, for stillbirths at 28 completed weeks gestational
age, the conventional gestational age-specific stillbirth rate is
the proportion of all births at 28 completed weeks that are
stillborn. Thus, the proportion is conditional on birth at 28
weeks of gestation. Although such a proportion is not inher-
ently “wrong,” it is often used to reflect the hazard (instanta-
neous risk) of stillbirth in gestations that have reached 28
weeks. Clearly, however, the gestational age-specific still-
birth proportion does not denote such a hazard. The hazard
should be composed of a numerator that denotes the number
of persons who experience the outcome at the specified gesta-
tional age and a denominator that includes all persons at risk
of developing the outcome at that gestational age. Above and
beyond the problems of definitions and applications of defini-
tions discussed in the previous section, the numerator of this
risk expression is fairly straightforward. However, the
denominator, that is, the population at risk, requires inclusion
of all those fetuses at risk of stillbirth (equivalent to number
of ongoing pregnancies for singleton gestations) between 28
0/7ths and 28 6/7ths completed weeks of gestation. In prac-
tical terms, this means taking the sum of stillbirths and live-
births at 28 weeks plus all fetuses remaining in utero (i.e., all
livebirths and stillbirths occurring at 29 or more completed
weeks of gestation) to calculate the denominator.

The importance of using the correct denominator is illus-
trated in figure 1, which is based on Canadian singleton
births from 1991 to 1998. When one compares the gesta-
tional age-specific hazard, as defined in the preceding para-
graph, with the gestational age-specific proportion of
stillbirths to stillbirths plus livebirths, one gets completely
opposite views of how the risk changes with advancing
gestation. The true risk (hazard) increases markedly as gesta-
tion advances, with the highest risk observed in the postterm
period. When expressed as the proportion of all stillbirths
and livebirths, however, the gestational age-specific rate of
stillbirths appears to decrease with advancing gestation.
Preterm birth cannot be a “cause” of stillbirth; rather, it is the
timing of the stillbirth that “causes” the preterm birth. These
contradictory perceptions of risk of stillbirths were recog-
nized by Yudkin et al. (27) more than 15 years ago, yet
continue to be ignored by many perinatal researchers (20,
28–30). Thus, when stillbirths are combined with early
neonatal deaths as “perinatal deaths,” the gestational age-
specific rates reflect an appropriate denominator for the early
neonatal deaths but an inappropriate denominator for the
stillbirths.

FIGURE 1.  Hazard (per 100,000 fetuses at risk) versus proportion (per 1,000 total births) representations of stillbirth risk in Canada, 1991–
1998.

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In actual practice, most perinatal researchers analyze perinatal mortality as a function not of gestational age, but rather of birth weight. Because errors in estimation of gestational age are known to be frequent, perinatal epidemiology has had a long history of examining birth weight-specific risk in addition to overall risk. Superficially, birth weight-specific stillbirth or perinatal mortality rates appear not to suffer from the same interpretational problems as gestational age-specific rates. However, the same problem exists here because gestational age is the primary determinant of birth weight, and birth weight-specific fetal or perinatal mortality conditions on births occurring within a given range of birth weight. Since fetuses of other (particularly larger) birth weights are at risk for stillbirth and yet are excluded from the denominator of stillbirths or perinatal mortality rates if they are neither liveborn nor stillborn while they “pass through” the given birth weight range during fetal development, the ratio of perinatal deaths to total births in that birth weight range does not reflect true risk. Moreover, birth weight-specific stillbirth or perinatal mortality rate has an additional problem: It conflates gestational duration with fetal growth. Because restricted fetal growth is closely associated with stillbirth (12, 13, 16–19), the numerator of the birth weight-specific stillbirth or perinatal mortality rate includes many growth-restricted fetuses, whereas the denominator adds those liveborn infants in the same birth weight range, most of whom are more immature (i.e., are of a lower gestational age) and appropriately grown. The interpretation of such a rate therefore becomes difficult, if not meaningless.

**WHAT ARE THE ALTERNATIVES?**

In rural, developing-country settings where most births occur at home in the absence of trained birth attendant, it is often difficult to distinguish between stillbirths and liveborn infants who die soon after birth. Traditional birth attendants may also vary in applying the World Health Organization definition of a livebirth. In such settings, combining stillbirths and early neonatal deaths into the category of perinatal deaths may provide more consistent public health measure of pregnancy outcome. We believe that in more developed settings, however, the concept of perinatal mortality has outlived its validity. Given the differences in etiologic determinants and in denoting gestational age-specific risk, combining stillbirths and early neonatal deaths is of limited value. In our opinion, such a combination provides misleading, and often highly confusing, indices for public health surveillance, international comparisons, and etiologic research.

Instead, we advocate the separate reporting of stillbirths and early neonatal deaths. Stillbirths should be reported by gestational age, using the proper denominator of all fetuses at risk, that is, all ongoing pregnancies at that gestational age. They should be separated, wherever possible, into antepartum versus intrapartum stillbirths, which provide windows on access to and quality of prenatal and delivery care, respectively. Early neonatal deaths should be reported by gestational age among livebirths, as is current practice. Nevertheless, as we argue elsewhere (Joseph et al., Dalhousie University, unpublished manuscript), quantifying the risk of neonatal death from the standpoint of all fetuses at risk can provide a distinct conceptual advantage.

Countries and regions within countries should conduct regular audits of registration practices to determine geographic and temporal trends in the occurrence of livebirths and stillbirths near the limits of viability, for example, at 20–25 completed weeks of gestational age. A helpful index for assessing whether the registration of births as stillbirths versus livebirths differs across geographic regions or over time is to examine the ratio of stillbirths to livebirths plus stillbirths in this gestational age range. Such differences usually reflect variations in completeness of registration, although in jurisdictions without separate registration of pregnancy terminations (induced abortions), late terminations (especially for congenital anomalies) may be partly responsible (31, 32).

In addition to documenting changes in trends in registration, the reasons for those trends should also be investigated. Possible reasons include changing (i.e., diminishing) limits of viability, as well as cultural, religious, and economic factors that favor registration versus nonregistration of borderline-viable infants as stillborn or liveborn.

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