Challenges in Improvement of Perinatal Health in Developing Nations

Role of Perinatal Pathology

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Maternal, fetal, and infant morbidity and mortality are among the most significant public health problems in developing and resource-poor nations. The World Health Organization (WHO) estimates that more than 9 million infants die before birth, or in the first few weeks of life each year, and that nearly all of these deaths occur in developing countries. In most developing countries, a large number of maternal and infant deaths escape diagnosis because of inadequate surveillance and reporting systems. Many of these deaths are caused by infectious diseases; others are the result of such pregnancy-related complications as placenta previa and abruptio placentae, multiple gestations, intrauterine growth retardation (IUGR), as well as delivery-related complications including intrapartum asphyxia, birth trauma, dystocia, fetal distress, preterm delivery, and premature birth. Some involve the health delivery system, including delayed admission to a delivery area and lack of transportation, essential obstetric and perinatal skills among caregivers, and equipment. Important contributing factors to maternal and perinatal morbidity and mortality in developing nations are the lack of adequate diagnostic and pathology facilities, inadequate or absent postmortem examination, poor diagnostic pathology and microbiology capabilities, and deficiency in surveillance systems, statistical reporting, and diagnostic accuracy of adverse maternal and perinatal health events. In most developing nations, individual pathologists, regardless of their training, must address all the numerous anatomic pathology, laboratory, diagnostic, forensic, and teaching responsibilities—and some nations may have only a few trained pathologists within their borders. Thus, most resource-poor nations of the world have no pathologist trained in perinatal pathology who is available to address the clinical, diagnostic, public health, and research aspects of fetal, infant, and maternal morbidity and mortality, which are so prevalent in these nations. Sadly, very few programs currently exist to specifically target perinatal and neonatal mortality, much less to train pathologists in perinatal pathology. The following sections highlight some of the most important perinatal health problems in developing nations, which would benefit by increased contributions from clinical, epidemiologic, and research collaborations with physicians trained in perinatal pathology.1-4

Malaria

Each year approximately 50 million women living in malaria-endemic countries throughout the world become pregnant. Malaria occurring during pregnancy remains one of the most important public health problems in parts of the world where Plasmodium spp infection is endemic. This is especially true in sub-Saharan Africa, where it affects an estimated 24 million pregnant women; malaria prevalence may exceed 50% among primigravid and secundigravid women in malaria-endemic areas.5 It is widely recognized that malaria has a detrimental effect on pregnancy outcome for both mother and infant: pregnant women with little or no preexisting immunity are at high risk for cerebral malaria, hypoglycemia, pulmonary edema, severe hemolytic anemia, and death. The link between malaria and perinatal morbidity/mortality is less clear in areas with stable endemic malaria where Plasmodium spp infection is endemic. This is especially true in sub-Saharan Africa, where it affects an estimated 24 million pregnant women; malaria prevalence may exceed 50% among primigravid and secundigravid women in malaria-endemic areas.5 It is widely recognized that malaria has a detrimental effect on pregnancy outcome for both mother and infant: pregnant women with little or no preexisting immunity are at high risk for cerebral malaria, hypoglycemia, pulmonary edema, severe hemolytic anemia, and death. The link between malaria and perinatal morbidity/mortality is less clear in areas with stable endemic malaria where pregnant women have acquired immunity.6 Malaria infection can cause low birth weight (LBW), and possibly abortion and stillbirth. The mean birth weight of infants born to mothers with placental malaria is reduced by 55 to 310 g. Low birth weight is more frequent in primigravidae with placental malaria than without placental malaria. Placental malaria is responsible for up to 35% of preventable LBWs in malaria-endemic areas. In malaria-endemic African countries, at least 13% of all infant deaths can be attributed to LBW resulting in 62000 to 363000 infant deaths per year. A recent review analyzing the malaria-infected population’s attributable risk for anemia (3%-15%), LBW (8%-14%), and infant mortality (3%-8%) estimated that each year between 75000 and 200000 infant mortalities.7

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The incidence of perinatal mortality caused by malaria is estimated to be 25 to 80 per 1000 per year in endemic nations.\textsuperscript{7–13}

**LOW BIRTH WEIGHT & IUGR**

Low birth weight, or birth weight less than 2500 g, is one of the principal contributors to neonatal morbidity and mortality worldwide, and accounts for up to 70% of neonatal deaths in some countries. About 20 million infants, or about 23.8% of all births, are born each year at a low birth weight. Infants with low birth weight are 20 times more likely to die than are normal-birth-weight infants. Those who survive may have impaired immune function and face increased risk for disease, including diabetes and heart disease later in life. They are also likely to remain malnourished and to have lower IQ and cognitive disabilities leading to school failure and learning difficulties. More than 95% of low-birth-weight babies are born in developing countries; however, data collection for low birth weight is difficult in resource-poor regions of the world because many babies are not weighed at birth. Worldwide, nearly 4 million babies die in the first month of life—low birth weight and premature birth are major causes. Half of all low-birth-weight babies in the world are born in South Central Asia, where 27% of infants (9.3 million infants) are born with a weight below 2.5 kg. The prevalence of low birth weight levels in sub-Saharan Africa is approximately 15% (3.1 million infants), and in the Caribbean, 14%.\textsuperscript{14–15}

Intrauterine growth retardation is the most common form of LBW in the developing world (accounting for more than 60% of the LBWs), whereas low birth weight in infants in developed countries is mostly due to prematurity. Risk factors for IUGR include a variety of chronic placental conditions resulting in uteroplacental malperfusion, cigarette smoking, low prepregnancy maternal weight and height, and low caloric intake and poor weight gain during pregnancy (see below). Importantly, the problem of low birth weight is intergenerational: low-birth-weight infants in resource-poor regions tend to remain suboptimally nourished during childhood and grow up to be malnourished adults who in turn give birth to small infants, thus perpetuating the cycle.

**MATERNAL MALNUTRITION**

Women of childbearing age (especially pregnant and lactating women), infants, and young children are in the most nutritionally vulnerable stages of the life cycle. Maternal malnutrition is a major predisposing factor for morbidity and mortality among women in resource-poor regions, especially Africa. The causes include inadequate food intake, poor nutritional quality of diets, frequent infections, and short interpregnancy intervals. Evidence for maternal malnutrition is provided by the fact that between 5% and 20% of African women have a low body mass index as a result of chronic hunger. Across the African continent the prevalence of anemia ranges from 21% to 80%, with similarly high deficiency for both vitamin A and zinc. Another public health problem in pregnant women is the high rate of human immunodeficiency virus (HIV) infection, which compromises maternal nutritional status. HIV infection has worsened the nutritional profile of African women. About 13.1 million African women aged 15 to 49 years live with HIV/AIDS, which coupled with poor nutritional status, quickly precipitates maternal malnutrition.\textsuperscript{18,29}

Maternal malnutrition before or during pregnancy can lead to spontaneous abortion, stillbirth, small-for-gestational-age and LBW babies, preterm delivery, and increased risk of perinatal and neonatal death. Also, certain forms of maternal malnutrition limit neurologic development in the fetus. Furthermore, maternal malnutrition may increase the risk of maternal infection and impair development of the fetal immune system. In resource-poor nations, at least 20% of the burden of disease in children younger than 5 years is related to poor maternal health and nutrition, as well as the quality of care during the neonatal period.

**HUMAN IMMUNODEFICIENCY VIRUS/AIDS**

HIV/AIDS is an increasing threat to the health of pregnant women and their infants in resource-poor regions. Mother-to-child transmission of HIV in developing nations, especially in those countries where HIV infection is continuing to increase in prevalence or has stabilized at very high levels, continues to be a major public health problem. In some areas, mother-to-child transmission of HIV occurs in 45% of pregnancies. HIV is a major cause of maternal mortality, causing 60,000 maternal deaths in 2008. HIV rates are especially high in sub-Saharan and Eastern Africa, where maternal mortality rates are on the rise. In the 5 countries with the highest adult HIV prevalence worldwide, HIV is the single leading cause of mortality in children younger than 5 years and is responsible for 41% to 56% of deaths.\textsuperscript{20}

In many other countries in sub-Saharan Africa, death certificate misclassifications underestimate mortality attributed to HIV/AIDS by as much as 53.1%.\textsuperscript{21,22} The cause of death is often classified as an opportunistic infection related to AIDS, but without reference to HIV. Despite the potential inaccuracies in HIV/AIDS statistics that underestimate prevalence and mortality, absolute HIV numbers are not decreasing. One thousand children were born with HIV infection each day in 2007, due in part to the fact that fewer than 25% of all HIV-positive women worldwide have access to prevention of mother-to-child transmission of disease. Of children born with HIV today in Africa, only 20% are expected to survive until their second birthday without highly active antiretroviral therapy.\textsuperscript{23}

The impact of HIV/AIDS on maternal and infant health in resource-poor nations cannot be overstated. HIV-positive children and their infected mothers are not the only victims of this epidemic. All children born to HIV-positive mothers (who, in some regions of Africa, constitute 25% of childbearing women) are at a higher risk for morbidity and mortality if maternal HIV is not treated effectively. Health care workers are not exempt from the epidemic. A study in Zambia found that 40% of midwives were HIV-positive,\textsuperscript{24} and estimates place seroprevalence rates for all health care workers in South Africa at approximately 16%.\textsuperscript{25}

**WAR, POLITICAL TURMOIL, AND REFUGEES**

The magnitude of migration appears to be increasing owing to a variety of geographic, political, and climatic issues. Migration, and the factors causing it, has a complex effect on the health of women of reproductive age, and pregnant women and their infants in particular. They face health problems that are exacerbated by their inferior social status as well as by their unique biological characteristics.
Family cohesion is threatened by migration policies and contemporary migration patterns. Women migrants face barriers to economic mobility when they migrate, especially when they lose the status attached to their family positions. Migrant women may also face sexual abuse by employers in receiving countries and from personnel and inhabitants in refugee camps. Migration also fuels the sex tourism industry in developing as well as developed nations, with a corresponding increase in violence and sexually transmitted diseases. Adverse health conditions may result from voluntary and forced migration because of administrative obstacles to care, lack of awareness about available services, linguistic barriers, failure to make health issues a priority, and the inferior social status of women. Pregnancy outcomes and perinatal health indicators suffer as well, and crude death rates of refugees are higher than baseline rates in their countries of origin. Rape and prostitution also affect perinatal health among migrant women, and are key factors in transmission of sexually transmitted diseases, especially HIV/AIDS and syphilis, affecting not only pregnant women but also their infants. Breast-feeding practices can be compromised by the indiscriminate distribution of milk powder and supplementary foods in refugee camps or by adoption of the more “modern” habits of urban areas. While it can be difficult to perform comprehensive studies of these populations of women and their infants for geopolitical reasons, the studies that have been performed have demonstrated increased risk for poor obstetric outcomes in pregnant refugees, including increased rates of neonatal and maternal deaths. This relationship has been confirmed in Afghanistan, one of the largest populations of refugees in the world. In a study of reproductive health in 12 Afghan refugee settlements located in Pakistan, the leading causes of death among women of reproductive age (15 to 49 years) were related to pregnancy.26,27

MATERNAL DEATH

Maternal death remains a major public health problem in resource-poor regions. Although pregnancy is considered a physiological process in developed nations, for women living in certain parts of the world, and most women in Africa, pregnancy is a life-threatening event. According to the WHO, poor maternal health accounts for the fourth leading cause of death for women worldwide, after HIV/AIDS, malaria, and tuberculosis. The statistics are staggering: in the developing world, greater than 500,000 women die each year as a result of complications during pregnancy and childbirth. Approximately one-half of these deaths occur in sub-Saharan Africa and one-third in South Asia— together these 2 parts of the developing world account for 85% of all maternal deaths worldwide. Although there has been a decrease in overall maternal mortality in the past few years, 99% of all maternal deaths still occur in developing countries. In sub-Saharan Africa, a woman’s lifetime risk of dying as a result of pregnancy is 1 in 16, whereas in industrialized nations the risk is 1 in 8000. The leading causes of maternal death are different in developing nations and in industrialized countries. Hemorrhage is the leading cause of maternal death in sub-Saharan African (34%) and Asian countries (31%), while hypertensive diseases during pregnancy are more prominent in Latin America and the Caribbean (26%). Abortion-related deaths are highest in Latin America and the Caribbean (12%) and can be as high as 30% in some countries in this region. Maternal deaths due to sepsis are higher in Africa, Asia, Latin America, and the Caribbean than in developed countries. In adolescent girls in developing nations, complications from pregnancy and childbirth are the leading cause of death.28–33 Unfortunately, owing to the lack of accurate reporting data on maternal deaths in resource-poor nations, the true burden of maternal deaths and their etiology are uncertain. Maternal mortality is difficult and complex to monitor, particularly in settings where the levels of maternal deaths are highest. Information is required about deaths among women of reproductive age, their pregnancy status at or near the time of death, and the medical cause of death—all of which can be difficult to measure accurately, particularly when vital registration systems are incomplete. This is due to many factors, but contributing factors are the deficiency of pathologists trained in the evaluation of maternal death, and the lack of performance of postmortem examinations.

UNSAFE ABORTION

An unsafe abortion is defined as “a procedure for terminating an unintended pregnancy carried out either by persons lacking the necessary skills or in an environment that does not conform to minimal medical standards, or both.”34,35 Every year, worldwide, about 42 million women with unintended pregnancies choose abortion, and nearly half of these procedures, 20 million, are unsafe. Some 68,000 women die of unsafe abortion annually, making it one of the leading causes of maternal mortality (13%). Of the women who survive unsafe abortion, 5 million will suffer long-term health complications such as hemorrhage and sepsis. Abortion-related deaths leave 220,000 children motherless annually. The WHO estimates that every 8 minutes a woman in a developing nation will die of complications arising from an unsafe abortion. Because of cultural mores, religious beliefs, and governmental influence, pregnant women in developing nations are at higher risk than women in developed countries for seeking abortion outside of the traditional health care environment.36–38

The main causes of death from unsafe abortion are hemorrhage, infection, sepsis, genital trauma, and necrotic bowel. Data on nonfatal long-term health complications are limited, but those documented include poor wound healing, infertility, consequences of internal organ injury (urinary and stool incontinence from vesicovaginal or rectovaginal fistulas), and bowel resections. Other nonmeasurable consequences of unsafe abortion include loss of productivity and psychologic damage. The risks of maternal morbidity and mortality in unsafe abortion depend on what method of abortion is used, as well as on women's readiness to seek postabortion care, the quality of the facility they reach, and the qualifications (and tolerance) of the health care provider. Methods of unsafe abortion include drinking toxic fluids such as turpentine, bleach, or drinkable concoctions mixed with livestock manure. Other methods involve inflicting direct injury to the vagina or elsewhere—for example, inserting herbal preparations into the vagina or cervix; placing a foreign body such as a twig, coat hanger, or chicken bone into the uterus; or placing inappropriate medication into the vagina or rectum. Unskilled providers also improperly perform dilation and curettage in unhygienic settings, causing uterine perforations and infections. Methods of external injury are also used, such as jumping
from the top of stairs or a roof, or inflicting blunt trauma to the abdomen.

**CHALLENGES IN ASSESSMENT OF MATERNAL AND PERINATAL MORBIDITY: ROLE OF PERINATAL PATHOLOGY**

Skilled pathology expertise is crucial in the improvement of maternal and perinatal health in resource-poor nations. In developing nations it is difficult to measure the true burden of maternal and infant morbidity and mortality. Perinatal pathology is of critical importance because it provides accurate diagnosis of placental pathology, evaluation of aborted fetuses, and autopsy pathology of stillbirths, neonates, and women dying as a result of pregnancy. These data are important for determining the exact causes of perinatal and maternal morbidity and mortality in developing nations, which in turn guide health care policy, research initiatives, and apportionment of the limited health care funding available in these regions.

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Similar to the situation with maternal death, information on causes of perinatal death of the fetus and neonate is extremely important not only for management of future pregnancies but also for policy-making and planning, monitoring, and evaluation of health programs, as well as being necessary for field research, comparisons, and epidemic awareness. In developing countries, where most perinatal deaths are neither attended by doctors nor medically certified, this crucial information is usually incomplete, and perinatal pathology support would result in greatly improved diagnostic accuracy. A pathologist trained in perinatal pathology can determine the cause(s) of most stillbirths and neonatal deaths, especially when the results of a placental evaluation are integrated with a thorough autopsy and with clinical and laboratory findings.

The evaluation of the placenta by pathologists specially trained in this subspecialty provides valuable information about the etiology, duration, and severity of fetal illness. Accurate placental pathology diagnosis can clarify the causes of adverse obstetric outcomes; improve management of subsequent pregnancies for women at risk; assist in the understanding of antenatal and intrapartum events contributing to such morbidities as growth restriction, infection, and neurodevelopmental conditions; and direct health care priorities in resource-poor nations. Unfortunately, even in developed nations, the accuracy of placental pathology diagnosis is suboptimal when performed by general pathologists who do not specialize in perinatal pathology. In one study,29 placental diagnostic discrepancies were found to be present in 92.7% of placentas diagnosed by general surgical pathologists, after review of the slides by a specialist. In most resource-poor nations, placentas are usually not examined, and when they are, pathologists specially trained in placental pathology are usually nonexistent. An important component of strengthening perinatal pathology expertise in developing nations is to provide special training in placental pathology from experts in this field.

Finally, the educational advantages of providing skilled perinatal pathology cannot be overstated. Pathologists receiving training in perinatal pathology can be a resource to the clinical, medical, and nursing communities in their nations.

**References**

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