

**EDITORIAL**

**Global Burden of Neural Tube Defects, Risk Factors, and Prevention**

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**Abstract**

Neural tube defects (NTDs), serious birth defects of the brain and spine usually resulting in death or paralysis, affect an estimated 300,000 births each year worldwide. Although the majority of NTDs are preventable with adequate folic acid consumption during the preconception period and throughout the first few weeks of gestation, many populations, in particular those in low and middle resource settings, do not have access to fortified foods or vitamin supplements containing folic acid. Further, accurate birth defects surveillance data, which could help inform mandatory fortification and other NTD prevention initiatives, are lacking in many of these settings. The burden of birth defects in South East Asia is among the highest in the world. Expanding global neural tube defects prevention initiatives can support the achievement of the United Nations Millennium Development Goal 4 to reduce child mortality, a goal which many countries in South East Asia are currently not poised to reach, and the 63rd World Health Assembly Resolution on birth defects. More work is needed to develop and implement mandatory folic acid fortification policies, as well as supplementation programs in countries where the reach of fortification is limited.

**Key Words**

Neural Tube Defects; Birth defects; South East Asia

**Introduction**

Birth defects are a leading cause of death in the first year of life, and, for infants who survive there is an increased risk for long-term disabilities. Although prevalence estimates for birth defects and their related disabilities can vary by source and are often dependent on what conditions are included and how they are defined [1-4], the World Health Organization (WHO) estimates that, globally, birth defects affect an estimated 1 in 33 infants, result in 3.2 million birth defect-related disabilities every year, and account for an estimated 270,000 newborn deaths yearly [5]. These estimates, however, may be impacted due to the ‘paucity of data’ [6], particularly in low- and middle-resource countries. This lack of data stems from variability in, or lack of, vital registration, diagnostic capacity, and capability of

countries to capture birth defects, a lack of an established birth defect surveillance system [6]. Furthermore, even if a birth defects surveillance system exists, prevalence estimates may not include birth defects among stillbirths and elective terminations because no information is collected on stillbirths or elective terminations or birth defects are not identified among stillbirths or terminations. As a result, the global toll of birth defects remains underestimated.

As infant mortality due to diarrheal and infectious diseases declines in low and middle resource countries, there is an increasing visibility of under-5 mortality due to birth defects [7]. Morbidity due to birth defects is also an important consideration, since, as medical technology continues to evolve, survival rates among babies born with birth defects

will likely increase. This will require that countries allocate significant financial resources to account for the long-term care for individuals with disabilities. According to the WHO, almost all (94%) severe birth defects occur in low- and middle-resource countries, due often to maternal malnutrition and exposure to teratogenic agents such as alcohol and tobacco. Other known risk factors associated with birth defects include micronutrient insufficiency and deficiency, maternal illnesses such as diabetes, overweight and obesity, and the use of certain medications during pregnancy [8]. Some risk factors might not be fully modifiable. Many require altering a behavior, such as abstaining from alcohol or tobacco use, changing medications prior to pregnancy, better disease management, or consuming folic acid supplements or fortified foods. The March of Dimes' Global Report on Birth Defects ranks countries by birth defects prevalence from a low of 39.7 per 1000 live births (France) to a high of 82 per 1000 live births (Sudan). Eight countries (India, Sri Lanka, Thailand, Nepal, Indonesia, Bangladesh, Myanmar, and Bhutan) in the South-East Asia region rank among those with birth defects prevalence estimates between 55 and 65 per 1000 live births [6]. In the region, the most common are birth defects of the cardiovascular system and neural tube defects (NTDs) [9]. NTDs are serious birth defects that occur when the neural tube, which ultimately will form a baby's brain and spine, fails to close properly. NTDs, although largely preventable, are a significant cause of death and lifelong disability worldwide. Globally, there are more than 300,000 babies born with NTDs each year [6]. NTD's occur widely and among diverse populations, with varying levels of economic development, and in different geographic areas [10]. The two most common NTDs are spina bifida and anencephaly [11].

The process of developing the neural tube is completed by day 28 of gestation. Spina bifida results from the failure of the formation of the vertebral column that protects the spinal cord. It can happen anywhere along the spine, and causes a range of lifelong disabilities including paralysis [11,12]. The lifetime direct cost of care for one child born with spina bifida in the United States is estimated to be \$768,000 [13]. There also are great social and emotional costs for children with spina bifida and their families. Anencephaly is a fatal birth defect that

occurs when the upper part of the neural tube does not fully close. Infants with anencephaly are often born without part of the skull and brain and die shortly after birth [12]. Folic acid deficiency or insufficiency puts a woman at higher risk for having a pregnancy affected by a neural tube defect. Although the majority of neural tube defects are preventable through the consumption of the synthetic B vitamin folic acid, because the neural tube closes by the 28th day of gestation, the window of prevention opportunity is limited. Other risk factors for neural tube defects are exposure to certain medications (e.g., valproic acid), certain chronic diseases (e.g., diabetes and obesity), and vitamin B12 deficiency [8].

In 1992, the U.S. Public Health Service recommended that all women of childbearing age capable of becoming pregnant consume 400 micrograms of folic acid daily to prevent neural tube defects. This recommendation was later followed by a mandate by the U.S. Food and Drug Administration for the fortification of cereal grain products labeled as enriched [14]. In the United States, mandatory fortification has led to a significant decrease (36%) in rates of neural tube defects [10], and a \$995 million estimated yearly savings resulting from folic acid mandatory fortification [13]. Mandatory fortification in the U.S. has proven to be an effective way to increase a woman's intake of folic acid without changing her dietary habits. Although countries such as Chile, South Africa, Canada, and Costa Rica have implemented mandatory fortification programs and have seen a significant decrease in neural tube defects as a result [10], in South East Asia, only Indonesia and Nepal currently have mandatory flour fortification policies in place [15]. According to estimates by Youngblood et al. (2012), only 25% of folic acid-preventable neural tube defects worldwide are being prevented [16].

## Conclusion

In summary, NTDs are common types of birth defects, the majority of which can be prevented with adequate intake of folic acid in the peri-conceptual period. Expanding the reach of global folic acid fortification in countries can lead to the prevention of 150,000–210,000 neural tube defects each year [10], or an estimated 13% of neonatal deaths attributed to birth defects in low resource countries [17]. It can also support the achievement of the

United Nations Millennium Development Goal 4 to reduce child mortality and the 63rd World Health Assembly Resolution on birth defects. Although progress has been made in addressing infant mortality, and successes have been achieved, many countries in South East Asia are currently not poised to reach Millennium Development Goal 4 [9]. More work is needed to advance the development of mandatory fortification policies to realize the broad implementation of fortification with folic acid and other micronutrients. By building on the successes in countries where it is a reality, mandatory fortification of staple foods with folic acid can be implemented and expanded to other countries and regions. Furthermore, efforts are needed to improve existing or to develop and implement new effective and sustainable folic acid supplementation programs in countries where fortification might not be feasible or where access to fortified products by the population is limited.

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