phg hna toolkit | Congenital Disorders

Background information on Neural Tube Defects and the impact of interventions

This document gives a brief overview about the condition, its epidemiology and specific interventions that may reduce its burden.

What are Neural Tube Defects?

Neural tube defects (NTDs) are complex congenital malformations of the central nervous system (CNS) caused by incomplete closure of the neural tube. They include spina bifida, encephalocoele (e-coele) and anencephaly. Those with anencephaly are stillborn or die shortly after birth; spina bifida and encephalocoele are compatible with life, but most affected infants are likely to have severe physical and mental disabilities. Although the majority of NTDs are non-syndromic, they can also be a feature of some syndromes such as trisomy 13; this document focuses on NTDs that are not part of specific genetic syndromes.

What are the main risk factors?

NTDs are thought to be caused by a combination of genetic and environmental factors. The most common risk factor is maternal folate deficiency; however, the mechanism by which folate prevents NTDs is not known. The risk when a previous child or one of the parents has the condition is 4% to 5%[1]. Rare genetic disorders, maternal diabetes, use of some medications such as folate antagonists e.g. valproic acid or carbamazepine in pregnancy, and other teratogens may also increase the risk of the condition in the offspring.

Global epidemiology

Birth prevalence

The birth prevalence of NTDs varies with countries and can change over time. According to the Modell Database of Constitutional Congenital Disorders (MGDB), the world-wide prevalence of non-chromosomal NTDs is 2.37/1,000. Data contained within PHGDB relate to isolated NTDs, i.e. those not associated with chromosomal disorders or other malformations. These have a worldwide prevalence of 2.21/1,000. It is estimated that approximately 184,910 live births in 2010 were affected by an isolated NTD. Another 71,961 are stillborn

[1] Milunsky A, Cannick J. Maternal serum screening for neural tube and other defects. In: Milunsky A, Milunsky J, editors. *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*. Wiley-Blackwell; 2010:705-771.

(0.60/1,000 births). Most affected births (in absolute numbers) are in the Asian continent, particularly in the South and East, and a significant proportion are born in Africa.

Population prevalence

The population prevalence in each country depends on the country specific population age distribution, proportion of affected pregnancies that are terminated, birth prevalence, retrospective life expectancy, and type and quality of treatment and care, including if and when any treatment policy was introduced.

Mortality

The condition contributed to around 162,007 under-5 deaths per in 2010, about half of these in South Asia.

Disability and quality of life

Improved perinatal, neonatal and neurosurgical care reduces early mortality associated with NTD. Surviving infants have a range of severities from none to severe cognitive and physical disability, depending on the severity of the defect and the impact of postnatal management. They require follow-up and care throughout life to treat complications including infections and possible neurological lesion as well as any associated physical disability or intellectual impairment.

Reducing prevalence, morbidity and mortality

Figure 1 illustrates the determinants and interventions for NTD as they relate to key stages in life. The main specific interventions are discussed below.

Interventions before pregnancy

These include the maintenance of good periconception folate nutrition, folic acid food fortification aimed at the whole population, and supplementation in the form of folic acid pills, either to all women or those in the preconception period.

Folic acid fortification of foods is a very effective intervention to reduce the birth prevalence and severity of NTD. Mandatory folic acid fortification of foods could reduce the NTD birth prevalence to 0.5 to 0.9/1,000, with the remaining cases being 'folate resistant'[2]; however this is hard to achieve and is also dependent on the baseline prevalence of the condition. For optimum results, it requires fortification of food staples that are widely consumed across the country or target population. In countries where it has been implemented, the incidence of NTD has been reduced by between 14% and 46%. As of June 2010, just over a quarter of the world population had access to folic acid fortified foods. For country specific data on food fortification go to http://www.sph.emory.edu/wheatflour/index.php.

Dietary supplementation with folic acid pills, started at least a month before conception and continued until 12 weeks gestation, is very effective at the individual level, but good population coverage is dependent on effective strategies to implement such programme. In optimum circumstances, it may reduce the risk of NTD by 62% (95% CI: 49% to 71%)[3].

[2] Wyszynski D (ed). *Neural Tube Defects: From Origin to Treatment*. 2006 Oxford University Press.

[3] Blencowe H, Cousens S, Modell B, Lawn J. Folic acid to reduce neonatal mortality from neural tube disorders. *Int J Epidemiol* 2010;39 Suppl 1:i110-i121.

Interventions during pregnancy

Prenatal care involves screening and diagnosis during pregnancy. This allows planning for a future baby with a congenital disorder or, in places where it is legal and acceptable, may lead to a choice of pregnancy termination. Worldwide, prenatal screening usually has high coverage. However, the quality of the services is variable and often poor, and state funded screening for anomalies is not common practice in many areas with less developed health services. Prenatal screening may involve different methods, for example maternal serum alpha fetoprotein (MSAFP) measurement or fetal ultrasound scan (USS). Confirmation of diagnosis involves ultrasound and less commonly amniocentesis. MSAFP at 16 weeks gestation has been linked with a detection rate of 82% and a false positive rate of 1.6%, but it does not detect closed defects. Anencephaly can be detected by ultrasound from 11 to 12 weeks of gestation; and spina bifida, from 16 weeks or earlier (from 13 weeks) for large defects. The sensitivity of USS in unselected populations has been reported as 98% for anencephaly, but is variable (65% to 90%) for other NTDs.

Interventions after birth

Care of people with a NTD requires a multidisciplinary approach involving both specialists and generalists for surgery, treatment of complications, rehabilitation, and social support. No treatment is available for anencephaly, which often leads to stillbirths or is lethal in the early neonatal period. Life expectancy can be estimated based on quality of care, and improves as care improves. Minimally treated infants with NTDs have a very short life span with severe illness. Death after the first year is usually due to meningitis, hydrocephalus or urinary tract infection. Disability and quality of life varies, depending on disease severity, capacity of health services and timeliness and quality of treatment of conditions and their complications. Surgery can improve the survival and quality of life of those with spina bifida and e-coele. However, the outcome of surgery is variable and depends on the severity of the defect and complications during and following the procedure, experience of the surgical team and health and support services infrastructure.

Cost-effectiveness of interventions

Folic acid supplementation and food fortification are among the most cost-effective public health interventions available. Fortification is relatively inexpensive, although costs vary internationally and with time. As an example, in Chile fortifying flour with folic acid has been estimated to save US$11.8 in medical costs for each dollar spent on fortification. If only one to two cases of NTD were prevented in a year (and many more are), this would have recovered the entire annual cost of fortification with folic acid in that year. In the US, folic acid fortification has been estimated to save US$145 million per year in costs for the care of children born with spina bifida. Prenatal screening and diagnosis also tend to be cost-effective interventions. It is important to note that cost-effectiveness of interventions varies geographically. For the economic benefits of food fortification, see the flour fortification initiative website http://www.sph.emory.edu/wheatflour/economicbenefit.php or the following http://www.foodstandards.gov.au/_srcfiles/P295%20Folate%20Fortification%20FFR%20Attach%202%20FINAL.pdf.

In the US, the average lifetime cost for medical treatment, educational services and lost productivity for one individual with spina bifida in 2002 was estimated to be US$635,763[4]. Treatment and care services for individuals with NTDs require a multidisciplinary approach and the availability and cost of these services can have global variations. For cost-

[4] http://health.utah.gov/birthdefect/defects/neural.html

effectiveness cut-off points for different regions of the world, go to http://www.who.int/choice/costs/CER_levels/en/index.html, and for costs for specific items by region and county, go to http://www.who.int/choice/costs/en/.

What are the main ethical legal and social issues (ELSI) to consider?

The ethical basis for state intervention

When public health interventions, such as folic acid fortification of foods, are targeted at populations rather than individuals the intrusiveness of the intervention, and any risks associated with it, should be balanced against the likely benefits, particularly if a degree of coercion is involved.

Current evidence suggests folic acid fortification and supplementation are very safe interventions, especially with intake levels of up to 1 mg/day of folic acid. Daily intakes under 5 mg/day are also likely to be safe. Fortification in high-malaria environments still needs to be examined. Caution has been recommended in these areas. This is because iron, which is often combined with folic acid in food fortification, may increase risk of death in malarial areas; and high doses of folic acid may reduce the efficacy of some antimalarials, such as sulfadoxine and pyrimethamine. At the time of writing, there seems to be no evidence that folic acid in doses used for fortification increases the risk of missing a diagnosis of vitamin B12 deficiency and associated neuropathy. Doses up to 1 mg/day have not been associated with clinically significant drug interactions and can be safely used in controlled epilepsy.

Those that oppose fortification programmes argue that such policies deprive competent adults of the chance to make an autonomous choice. This is particularly the case if all potential sources of a particular product are fortified. As some types of food are less amenable to folic acid fortification than others (for example wheat is more easily fortified than rice), and as some people, usually the most isolated and the less well off in society may not have access to fortified products (e.g. by relying on subsistence agriculture or local produced products) the exclusive use of food fortification may lead to an unfair distribution and access to the benefits conferred by the fortified foods.

It is possible to preferentially target those who are planning a future pregnancy, or at risk of becoming pregnant, by providing folic acid supplementation in the form of folic acid pills. However, such programmes may be less accessible to vulnerable groups or those of lower socio-economic class, raising issues of lack of equity in provision of the service.

Access to prenatal screening and termination of pregnancy

Disadvantaged groups may be less likely to have access to prenatal screening and termination services, particularly if, as in many low and middle income countries (LMIC), these services are funded privately.

In many LMIC legal termination of pregnancy is unavailable or severely restricted to cases where it is necessary to protect the woman's life. In some countries access to termination may also depend upon parental or spousal consent. In practice, in many countries, the majority of procedures are offered illegally, often by unqualified practitioners, and may cause substantial physical and psychological harm.

Exercising a parental choice to continue with an affected pregnancy

There is sometimes concern that it may be difficult for mothers who have an affected child identified on screening to choose to proceed with the pregnancy (with the resultant burden that is likely to impose upon themselves, family, health providers and state).

Living with a disability

Those who are born disabled often have a very poor life expectancy, especially in LMIC. This is due to a combination of factors: lack of access to relevant health and social services compounded by social disadvantages such as poverty and poor education. Affected individuals may experience stigma, discrimination and psychological difficulties.

KEY REFERENCES

Blencowe H, Cousens S, Modell B, Lawn J. Folic acid to reduce neonatal mortality from neural tube disorders. *Int J Epidemiol* 2010;39 Suppl 1:i110-i121.

Boyd PA et al. Evaluation of the prenatal diagnosis of neural tube defects by fetal ultrasonographic examination in different centres across Europe. *J Med Screen* 2000;7:169-174.

Flour fortification initiative (http://www.sph.emory.edu/wheatflour/index.php).

Lawrence M. Challenges in translating scientific evidence into mandatory food fortification policy: an antipodean case study of the folate-neural tube defect relationship. *Public Health Nutrition* 2005;8:1235-1241.

Lumley J, Watson L, Watson M, Bower C, Dowswell T. Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. *Cochrane Database of Systematic Reviews*: Reviews 2001;(3).

Merkens, MJ (ed) for the Professional Advisory Council, *Guidelines for Spina Bifida Health Care Services Throughout the Lifespan*. Spina Bifida Association; 2006.

Milunsky A and Milunsky J. *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*. Wiley-Blackwell; 2010.

Wyszynski D (ed). *Neural Tube Defects: From Origin to Treatment*. Oxford University Press; 2006.

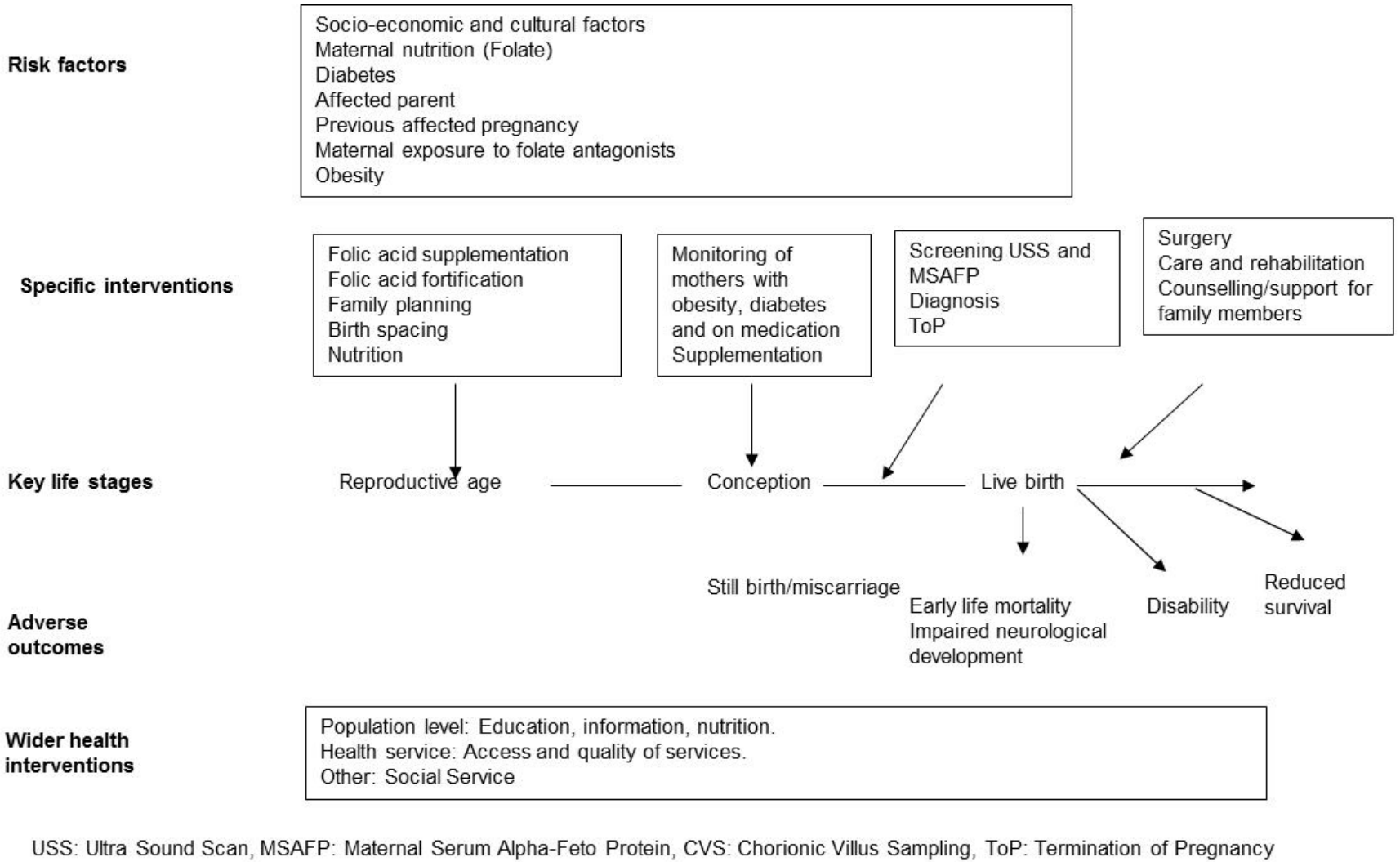
RELATED TOPICS

Preconception care and screening

Prenatal care and screening

Newborn screening

Figure 1: Needs assessment flowchart for Neural Tube Defects



USS: Ultra Sound Scan, MSAFP: Maternal Serum Alpha-Feto Protein, CVS: Chorionic Villus Sampling, ToP: Termination of Pregnancy