
Birth defects

Report by the Secretariat

1. This paper aims to inform the discussion on birth defects and congenital disorders, given their importance as a cause of stillbirths and neonatal mortality. According to the International Classification of Diseases Tenth Revision (ICD10), congenital anomalies include congenital malformations, deformations and chromosomal abnormalities, but exclude inborn errors of metabolism. Every year more than 7.9 million children – 6% of total births worldwide – are born with a serious congenital disorder due to genetic or environmental causes. The most common serious congenital disorders are congenital heart defects, neural tube defects and Down syndrome. Haemoglobinopathies (including thalassaemia and sickle cell disease) and glucose-6-phosphate dehydrogenase deficiency, which are not covered by the ICD10 definition of congenital anomalies, account for 6% of all congenital disorders. In addition, haemolytic disease of the newborn caused by Rhesus incompatibility, a preventable and relatively frequent disorder, is not included in the ICD10 definition of congenital anomalies. An expanded definition covers abnormalities of structure or function, including metabolism, which are present from birth, but irrespective of which definition is used, there is an immediate need to prevent and manage serious congenital disorders. They can be life-threatening, result in long-term disability, or both, and negatively impact individuals, families, health-care systems and societies.

CONGENITAL DISORDERS AND GLOBAL NEWBORN AND CHILD MORTALITY

2. Around nine million children continue to die every year. About 37% of these deaths occur within the first 28 days of life. Globally, the most common causes of neonatal deaths are infections, preterm birth and asphyxia. The most common causes of deaths from one month up to five years of age are pneumonia, diarrhoea, malaria, measles and HIV infection, with undernutrition contributing to about 35% of all deaths among children less than five years of age. In countries where the mortality rate in children under five years of age is relatively low (e.g. <30 per 1000 live births), neonatal deaths can account for more than 60% of all child mortality. Further, the distribution of the causes of death of neonates and infants aged 1–59 months shifts as child mortality levels decline, with, as a result, conditions such as congenital disorders, injuries and chronic diseases assuming much greater importance as causes of child mortality than infections and asphyxia.

3. According to *World health statistics 2008*,¹ about 260 000 neonatal deaths worldwide are caused by congenital anomalies. This figure represents about 7% of all neonatal deaths, but ranges from 5% in the South-East Asia Region to more than 25% in the European Region. Available data

¹ *World health statistics 2008*. World Health Organization, Geneva, 2008.

suggest large between-country variation: from 4% (Bangladesh, Equatorial Guinea, Ethiopia, Liberia, Mali and Sierra Leone) and an estimated 8% in China to 38% and more (Bahrain, Cyprus, Ireland, Kuwait, Qatar and Syrian Arab Republic). These percentages are likely to be underestimates because they rely on data from verbal autopsy studies, thereby resulting in some probable misclassifications of deaths due to congenital disorders such as congenital heart defects. Taken together, these figures indicate, in the context of achieving the target of Millennium Development Goal 4, namely, reduce by two thirds, between 1990 and 2015, under-five mortality rate, the need to reduce the rate of congenital anomalies. Control of congenital disorders assumes a higher priority in countries and settings with relatively low under-five mortality rates where 10% or more of all child deaths are expected to be caused by congenital anomalies. Congenital anomalies are also a leading cause of fetal death and an increasing cause of neonatal mortality in countries undergoing the epidemiological transition (for example, China). Although congenital anomalies account for a smaller percentage of deaths of neonates and infants aged 1–59 months in middle-income and low-income countries than in the wealthiest countries, more than 95% of all child deaths due to congenital anomalies occur in these settings, indicating that congenital anomalies affect all countries and represent a significant challenge to public health globally.

PREVENTION

4. The diversity of causes and determinants of congenital disorders requires a range of preventive and treatment approaches, some of which raise ethical and social issues. Means of preventing congenital disorders include:

- provision of family planning and other reproductive health care services, such as the prevention and treatment of vertically transmitted infections (e.g. syphilis)
- nutritional interventions, such as iodine fortification for the prevention of cretinism and folic acid supplementation or food fortification programmes for the prevention of neural tube defects (targeted at all women of child-bearing age)
- routine immunization for the prevention of rubella and varicella
- community education and education campaigns targeted at women of child-bearing age about the dangers of alcohol intake and consumption of medications with potentially teratogenic side-effects during early pregnancy
- provision of community genetic services within the primary health care system
- surveillance for congenital disorders.

PRECONCEPTION AND PRENATAL SCREENING AND GENETIC COUNSELLING

5. Preconception care (e.g. appropriate management of diabetes and other chronic diseases including obesity, and education about the risks associated with consanguinity), treatment of specific preventable diseases (e.g. congenital adrenal hyperplasia) and many of the presently recommended interventions for the control of congenital disorders form an integral part of comprehensive programmes for maternal and child health. Thus, controlling congenital disorders requires not the development of new programmes but better coordination of existing actions and programmes, such as

including folic acid in micronutrient fortification of staple foods, using the bivalent rubella/measles vaccine for routine immunization, and screening maternal serum during antenatal care. Such integration requires investment of time and effort and substantially increasing the capability of health-care professionals.

6. Genetic counselling should precede pre-marital screening and prenatal diagnosis of congenital disorders, and it should provide couples at risk with information on the expected reproductive outcomes and management options available for their pregnancies. Prenatal diagnosis focuses on the detection in utero of congenital disorders due to chromosomal abnormalities, single gene defects, multifactorial disorders and environmental determinants. Specific indications for prenatal diagnosis are pertinent to each of these categories. The most common is advanced maternal age, and other common indications are family history of a genetic disorder, specific ethnicities and populations in which the risk is increased, and teratogenic exposure. The procedures for prenatal detection of congenital disorders are usually carried out sequentially, starting with non-invasive screening and followed by progressively more invasive diagnostic techniques in cases with abnormal findings.

7. Minimally invasive screening methods that are currently available involve the measurement of several metabolites in the maternal serum. Abnormal levels of biochemical markers are also associated with fetal structural defects such as Down syndrome, neural tube defects and open ventral wall defects. The detection rate of congenital disorders in the first trimester through biochemical screening is improved when it is done in tandem with ultrasonographic screening for nuchal translucency and other ultrasonographic assessments.

8. Ultrasonography is used as a prenatal screening tool in the first trimester (at 11–13 weeks) for detection of fetal chromosomal abnormalities and major structural defects and in the second trimester (at 18–21 weeks) for detecting structural fetal anomalies. Evaluation of nuchal translucency at 11–13 weeks can detect 75% of trisomy cases and, when used with other measures such as biochemical tests and visualization of nasal bone, the detection rate can reach 95%. A dedicated anomaly scan at 18–21 weeks has very high detection rates for neural tube defects (open spina bifida, anencephaly, encephalocele) and for certain other congenital abnormalities (for example, gastroschisis, renal agenesis and skeletal dysplasias). The detection rate for congenital heart defects and other non-cardiac anomalies is variable but improving as experience grows and new technology becomes available.

9. More invasive prenatal diagnostic techniques are based on the sampling, culturing and karyotyping, and DNA analysis or metabolic assays, of embryos (pre-implantation diagnosis), chorionic villus cells, desquamated fetal cells in amniotic fluid, fetal blood and fetal tissue. These tests are performed in only a limited number of centres. The methods are associated with an increased risk of miscarriage (1% for amniocentesis and chorionic villus sampling). Programmes of prenatal screening and diagnosis have significantly improved the chances of at-risk couples having unaffected children.

10. Future diagnostic developments include the combination of different measures, such as biochemical screening and ultrasonography, and the introduction into clinical practice of new biomarkers and DNA analysis techniques, including analysis of cell-free DNA and RNA. These advances are expected to reduce progressively the use of invasive diagnostic techniques in favour of minimally invasive or non-invasive procedures.

DETECTION, TREATMENT AND CARE

11. Detection and treatment of congenital disorders can be promoted through the implementation of prenatal screening for congenital disorders (particularly ultrasonographical examination) and neonatal screening programmes (physical examination of all neonates, screening for congenital hypothyroidism, phenylketonuria, sickle cell disease and glucose-6-phosphate dehydrogenase deficiency) as well as training of primary care providers in the diagnosis and appropriate referral for treatment of infants with congenital disorders. Treatment options include in utero therapy and postnatal surgical corrections; these are being investigated and evaluated in a few selected centres for a number of conditions (e.g. congenital diaphragmatic hernia, congenital heart lesions, myelomeningocele, and twin-to-twin transfusion syndrome). Appropriate treatment and care are also needed for patients with impairments that become manifest after the neonatal period, and include early detection and treatment of physical, mental, intellectual or sensory impairments, and access to health and rehabilitation services in order to support participation and inclusion of affected children.

POTENTIAL ACTIONS

12. Several country-level actions have been identified that would ameliorate the prevention and management of congenital disorders:

- improving maternal health care services from preconception onwards
- strengthening family planning and reproductive health services
- implementing or increasing the coverage of specific preventive measures such as iodization of salt, folic acid fortification or folic acid supplementation of women of child-bearing age, universal vaccination against measles, mumps and rubella, education programmes, screening for alcohol consumption by women of child-bearing age and in pregnancy, interventions for hazardous and harmful drinking, and appropriate legislation for reducing tobacco use and harmful use of alcohol
- implementing health education programmes, both for general populations and targeted at high-risk groups
- strengthening prenatal screening for congenital disorders, coupled with effective information and counselling, including information on life with disabilities
- implementing neonatal screening and training primary-care providers in genetic risk detection and management and the diagnosis and appropriate referral for treatment of infants with congenital disorders
- strengthening treatment, medical care, surgical treatment and comprehensive rehabilitation services
- fostering the development and growth of parent–patient organizations in support of care and prevention programmes
- establishing community genetic services within the primary health care system
- establishing a surveillance system for congenital disorders.

13. Several actions have been identified that would improve the prevention and management of congenital disorders if implemented at the international level:

- promoting the collection of data on the global burden of mortality and disability due to congenital disorders. (Work to this end is under way and will focus on incidence rates and management options for severe maternal and newborn morbidity in 25 countries, 420 health facilities and 350 000 pregnancies.)
- revising ICD10 to broaden the groups of congenital conditions included in the classification
- promoting the strengthening of care and preventive services in lower-income countries
- promoting synergy and preventing duplication of activities through provision of information
- establishing training centres for ultrasonography and other diagnostic procedures
- advocating the importance of the prevention of congenital disorders and stimulating and coordinating research on cost-effective approaches and interventions for their prevention and control.

ACTION BY THE EXECUTIVE BOARD

14. The Board is invited to note this report and provide further guidance.

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