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Background information on Congenital Hypothyroidism 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 is Congenital Hypothyroidism?

The thyroid gland produces hormones involved in the control of metabolism in almost every cell in the body and is important for early growth and development, especially of the brain, as well as regular maintenance of physiological function. Congenital hypothyroidism (CHT) refers to under-activity of the thyroid gland present from birth. This can be caused by iodine deficiency, defects in the development of the thyroid gland or errors in thyroid metabolism. Hypothyroidism can lead to a number of functional and developmental abnormalities and can manifest in a number of ways including arrested physical and mental development, goitre, impaired cognitive function and growth and increased perinatal mortality and morbidity.

What are the main risk factors?

The most common cause of all forms of hypothyroidism world-wide is dietary iodine deficiency. Iodine is a vital component of thyroid hormones; therefore dietary intake is required for their adequate production. The developing fetus is dependent on maternal thyroid hormones during the first few weeks and, later in development, on maternal iodide for hormone synthesis. Consequently, maternal iodine deficiency can lead to fetal iodine deficiency and permanent brain damage in severe cases. Congenital hypothyroidism caused by lack of iodine is sometimes referred to as transient hypothyroidism and can be endemic in areas of iodine deficiency.

Hypothyroidism in individuals can be caused by lack of access to iodine fortified foods or consumption of goitrogens (substances that interfere with thyroid function). Transient hypothyroidism can also be caused by maternal iodine excess, use of iodide containing drugs during pregnancy, and antibodies that block thyroid stimulating hormone (TSH) (e.g. as a result of maternal Grave's disease). Some forms of CHT are permanent. These include CHT caused by sporadic or inherited mutations that affect thyroid development, function or metabolism, or autoimmune disease (e.g. Hashimoto thyroiditis or Grave's disease).

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Global epidemiology

Birth prevalence

The prevalence of CHT around the world varies, with a global prevalence of approximately 1/3000. However, environmental factors play an important role in birth prevalence with increasing rates in areas which have iodine deficiency where they may be as high as 1/900. Table 1 summarises the different forms of CHT in neonates and their estimated birth prevalence.

Global access to iodised salt

Iodine deficiency disorders have been eradicated in many industrialised countries due to iodine supplementation of food products for human and animal consumption. Salt iodisation is the most common means of dietary iodine supplementation, and many countries have implemented either voluntary or mandatory salt iodisation programmes. Progress has also been made in low- and middle-income countries (LMIC) following the implementation of national universal salt iodisation programmes. Household access to iodised salt varies from over 90% in America, Western Europe and Australia to less than 70% in parts of Africa and Asia, with 30% of the world's population still lacking access to iodised salt.

Clinical outcomes

Mortality and morbidity

Neonatal screening for thyroid hormones detects all forms of CHT and these respond well to hormone replacement therapy. The length of therapy will vary depending on the cause of the deficiency. Transient hypothyroidism will require short-term therapy as opposed to permanent forms of hypothyroidism. The most serious adverse effect of hypothyroidism is neurological damage; if therapy is not initiated in time, neurological damage can become permanent. Therefore, cases that are diagnosed late may require additional support and management throughout life, depending on the extent of neurological damage. Other, less severe symptoms include loss of physical and mental energy. Maternal iodine deficiency can have serious consequences for the developing fetus including spontaneous abortion.

Completely untreated CHT due to thyroid a/dysgenesis leads to cretinism, a very severe form of mental retardation. In settings without systematic social support for families, severe mental retardation usually leads to early death due to neglect in some form. Hence newborn screening and treatment services as well as social support is required to ensure those with CHT are able to achieve normal life expectance.

In the absence of accurate country-specific data on the global spread of neonatal screening and clinical outcomes of CHT, PHGDB mortality estimates are limited to those for CHT due to thyroid a/dysgenesis. This data therefore only applies to the most severe form of CHT.

Disability and quality of life

Treatment and care aims to minimise disability and improve quality of life. Identification of CHT and initiation of hormone therapy within two weeks of age can normalise cognitive development. Initiation of treatment up to the age of 3 years can reverse some of the signs and symptoms of hypothyroidism. Those with permanent CHT will require on-going therapy.

Reducing prevalence, morbidity and mortality

Reducing affected birth prevalence depends on ensuring iodine sufficiency, and newborn screening for CHT, which enables early diagnosis and treatment. Figure 1 illustrates the determinants and interventions for CHT as they relate to key stages in life. The main specific interventions are briefly discussed below.

Interventions before pregnancy and population wide

In most countries the primary means of preventing CHT as a result of iodine deficiency is through ensuring the availability of fortified food products - mainly iodised salt, which has been shown to be an effective and low-cost intervention. In the 1990s the World Health Assembly recommended the adoption of Universal Salt Iodisation (USI) as the method of choice to eliminate iodine deficiency disorders. (Iodisation of salt and population iodine levels are monitored to ensure that excessive consumption does not occur.) Other alternatives to salt iodisation are fortification of milk, water or bread. Currently, the main sources of iodine in industrialised countries are dairy products and grain and cereals. In areas without access to salt (due to their remoteness) or where salt iodisation programmes are unable to meet the needs of pregnant women, iodised oil as a supplement is an alternative.

Interventions during pregnancy

Knowledge of maternal health especially with respect to iodine deficiency, iodine excess or the use of iodide containing drugs help appropriate management in pregnancy. Management could involve iodine supplementation in cases where the mother is iodine deficient or management of anti-thyroid medication, as appropriate.

Interventions after birth

Screening for CHT is the most widely undertaken neonatal screening service in most countries and involves measurement of TSH and/or T4 (thyroxine, a thyroid hormone) in blood samples (usually dried blood spots from heel prick) using a radio-immunoassay. Treatment involves administration of thyroid hormone; the duration of this therapy varies depending on the specific cause of CHT (i.e. permanent or transient). Further management depends on the outcome of therapy.

Cost-effectiveness of interventions

Iodine supplementation and fortification are among the most cost-effective public health interventions available. Fortification of salt can cost as little 2-7 US cents per kg of salt.

Studies looking at cost-effectiveness of newborn screening in developed countries usually agree that screening is cost-effective and/or cost saving for certain conditions but not necessarily all. Results depend on the costs involved, test characteristics and the birth prevalence of the condition(s), as well as the number of conditions within the screening programme. Key to realising the benefit of screening is the ability to detect a condition at an early stage where treatment can potentially avoid or reduce sequelae of the disease. Economic evaluations carried out in high-income countries indicate that screening for CHT has a favourable cost:benefit ratio - savings made in medical care, special education and lost productivity among others outweigh the cost of the screening programme itself.

Countries are advised to undertake their own analysis that is relevant to their particular needs. For cost-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?

Iodine fortification

The fortification of food with iodine is an example of a public health intervention that is targeted at the whole population. It is justified on the basis that the benefits of reducing the prevalence of children born with iodine deficiency disorders outweigh any risks of the intervention. Although the WHO recommends universal salt iodisation, there are concerns that this may conflict with policies to reduce salt consumption. The exclusive use of food fortification may raise issues of lack of autonomy and distributive justice.

Newborn screening

Newborn screening raises several ethical and legal issues which must be considered, including equity of access, provision of adequate information about the screening process, and the availability of effective and affordable treatment.

Living with a disability and social support

CHT is associated with ongoing physical and behavioural disabilities if not diagnosed and treated early. Affected individuals may experience stigma and discrimination, as well as economic and social deprivation. In high income countries, the effect of severe physical or psychological disabilities may be ameliorated by support from the state, but this may be virtually non-existent in LMIC, where healthcare, education and social services are limited, and the burden of having a disabled child often falls entirely on the immediate and extended family.

KEY REFERENCES

Hetzel BS, Pandav CS, editors. *S.O.S For a Billion - The conquest of iodine deficiency disorders*. 2nd ed, 1996. Oxford University Press.

World Health Organisation. *Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers*. 3rd ed. 2007 Geneva: World Health Organisation..

International Atomic Energy Agency. Screening of Newborns for Congenital Hypothyroidism - Guidance for Developing Programmes. 2005. Vienna..

The International Council for Control of Iodine Deficiency Disorders : http://www.iccidd.org/

Rastogi MV and La Franchi SH, Congential Hypothyroidism Orphanet J Rare Dis. 2010: 10;5:17.

RELATED TOPICS

Preconception care and screening

Newborn screening

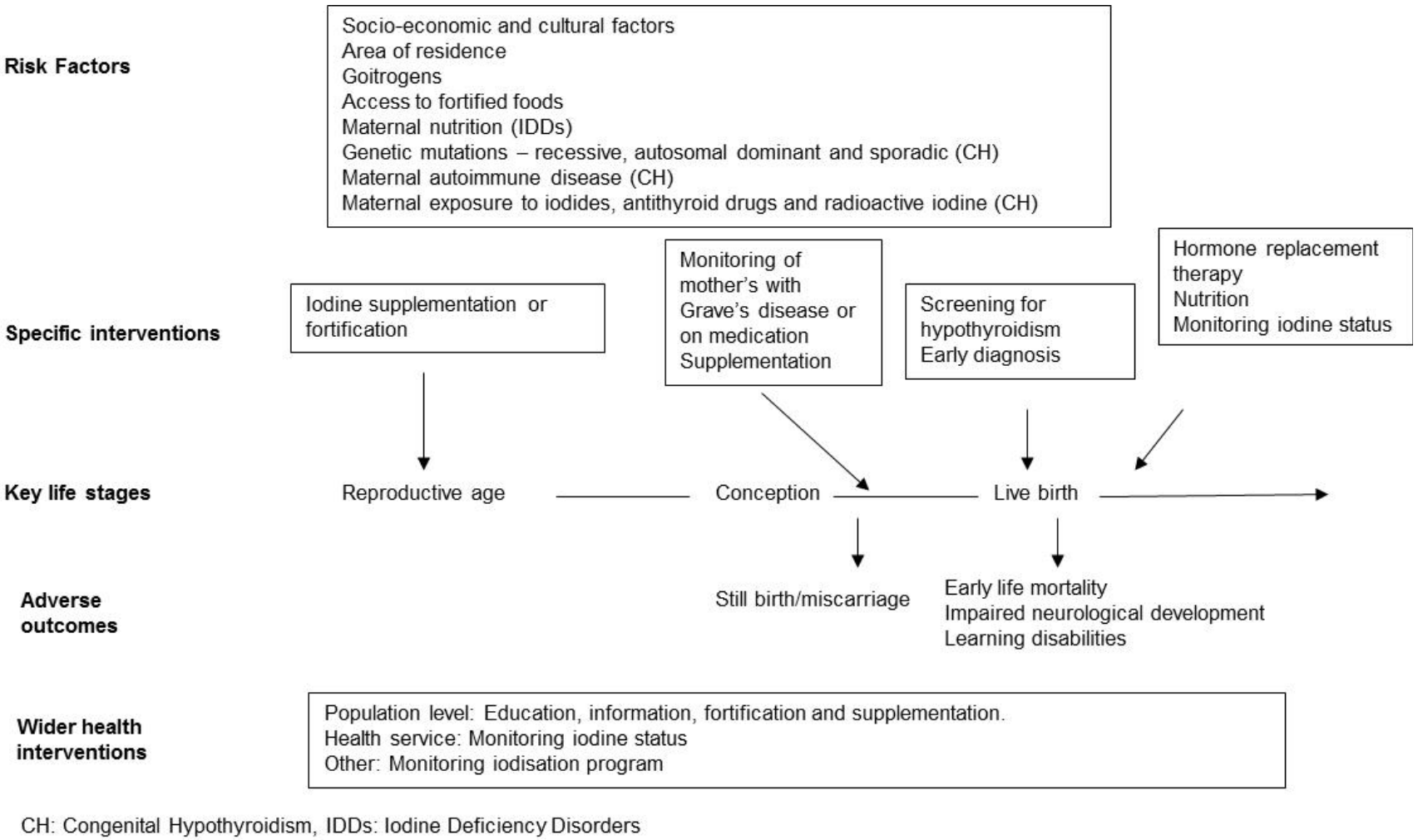
Teratogens

Table 1: Birth prevalence of different forms of congenital hypothyroidism[1]

Category of CHT	Pathology	Risk Factor(s)	Prevalence
Permanent CHT	Complete or partial absence of thyroid gland	Sporadic genetic mutations	1/3000-4000
	Errors in thyroid hormone synthesis	Inherited autosomal recessive mutation in enzymes involved in hormone synthesis	1/30,000
	Secondary hypothyroidism	Pituitary or hypothalamic abnormalities	1/50-10,000
	Thyroid hormone resistance	Inherited autosomal dominant mutation in thyroid receptor	1/100,000
Transient CHT	'Normal' thyroid gland but production of hormone is insufficient for a period of time	Prenatal or postnatal iodine deficiency	Variable
		Prenatal exposure to maternal anti-thyroid drugs	
		Maternal TSH receptor blocking antibodies	
		Prematurity	
		Maternal hyperthyroidism	

[1]Brown, RS., Disorders in the Thyroid Gland in Infancy, Childhood and Adolescence, in www.thyroidmanager.org, [date accessed: August 2010] Published by ENDOCRINE EDUCATION Inc, South Dartmouth, MA 02748

Figure 1: Needs assessment flowchart for congenital hypothyroidism



CH: Congenital Hypothyroidism, IDDs: Iodine Deficiency Disorders