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National Maternity Data Development Project

Research brief **no. 3**

Baby head circumference

Head circumference (HC) is an anthropometric measurement that can be used to assess whether an infant's head size is within the normal range for age. HC measurements at birth (together with weight and length) reflect intrauterine growth and allow for proper assessment of fetal growth. HC is also used as a proxy measure for brain development (both intrauterine and from birth), and can be predictive of some baby outcomes.

The World Health Organization (WHO) released a new international growth standard in 2007 showing how healthy children should grow. HC is measured according to percentiles that compare an individual's measurements with an appropriate age – and sex-specific growth chart. Percentile measurements are clinical indicators that rank the position of an individual's size and growth by indicating the percentage of the reference population an individual would equal or exceed. For example, 50% of the population are expected to be below the 50th centile; 90% below the 90th centile. One-half of all children at a given age are usually between the 25th and 75th centiles.

Various definitions of normal limits are found in the literature. In Europe, the 3rd, 10th, and 25th centiles below the mean, and the 75th, 90th and 97th centiles above it, are used to determine cut-off points. The 5th and 95th centiles have been more routinely used in North America. The World Health Organization recommends the use of standard deviations (SD) to determine normal limits (Amiel-Tison et al. 2002). However, no clear cut-off point that defines abnormal growth has been identified; some researchers use 2 or 3 standard deviations as abnormal growth cut-off points when examining head circumference.

Different growth charts (or curves) are applied to full-term and pre-term infants respectively, because pre-term infants at birth are smaller in size than fetuses of the same gestational age (Olsen et al. 2010). There is also a variety of growth charts in existence and it is currently unclear whether all Australian jurisdictions use the same growth standard.

Significance of head circumference to morbidity and mortality

The most dramatic increase in brain volume occurs in the period encompassing the last 3 months of fetal life and the first 2 years after birth (Amiel-Tison et al. 2002). HC changes over this period therefore provide an indirect measure of intrauterine and postnatal brain growth, and may be of prognostic significance in relation to later developmental outcomes. HC correlates closely with brain volume, and the relationship between head and brain growth is the reason why neurological assessment in infancy universally includes measurement of HC (Amiel-Tison et al. 2002).

Normal HC is generally within the range of 3rd–97th percentile (Khadilkar & Khadilkar 2011); however, depending on the risks being screened for, different cut-off points can apply. An HC less than the 3rd percentile is referred to as microcephaly, whereas an HC greater than the 97th percentile is referred to as macrocephaly. Both can be indicative of a potential problem. Classification of head growth into normocephaly, microcephaly, or macrocephaly often occurs at birth (Amiel-Tison et al. 2002). However, for some conditions being screened for (such as Fetal Alcohol Syndrome), cut-offs of 5th and 95th, or 10th and 90th percentiles apply.

For a healthy full-term infant, normal head circumference is approximately 33–37 cms at birth. Males tend to have an HC that is 0.5 cms larger than for females (Amiel-Tison et al. 2002).

For a healthy pre-term infant, HC is measured according to gestational age (Fenton & Kim 2013).

Microcephaly

Microcephaly refers to a condition in which HC is significantly smaller than average for the age and gender of an infant or child. Although <3rd percentile is commonly used to define microcephaly, some literature defines it also as <5th or <10th percentile. Microcephaly may be evident at birth or may become apparent during the first years of life. It usually occurs when the brain fails to grow at a normal rate, and as a result the infant's skull fails to expand normally.

Microcephaly is also said to be present when HC is more than 2 standard deviations below the mean for age and sex. However, many researchers use an HC of 3 standard deviations below the mean in determining microcephaly. Measurements below the 3rd percentile can indicate reduced brain volume (Barbier et al. 2013; Kuban et al. 2009; Kurtoglu et al. 2012) where infants and children are at risk of developing neurologic and cognitive disorders (Chung 2009). Multiple measurements of HC over time plotted against a standard growth chart provide important information for diagnosis and prognostication.

Microcephaly often occurs in pre-term babies, babies with very low birthweight, babies who experience intrauterine growth restriction (IUGR) or babies who are born small for gestational age (SGA) (Peterson et al. 2006). In babies who are born SGA, head circumference at birth can be a predictor of small head circumference at 6 months.

Though microcephaly is not a disease, it may be a signpost of conditions such as epilepsy, cerebral palsy, intellectual disability, developmental delay, and eye and ear disorders (Chung 2009). The frequency of these associated conditions varies depending on etiology. Depending on the severity of the accompanying syndrome, children with microcephaly may have mental retardation, delayed motor functions and speech, facial distortions, dwarfism or short stature, hyperactivity, seizures, difficulties with coordination and balance, and other brain or neurological abnormalities. Some children will have normal intelligence and a head that will grow bigger, but they will track below the normal growth curves for head circumference (National Institute of Neurological Disorders and Stroke 2013).

Small head circumference is related to Fetal Alcohol Syndrome Disorder (FASD), and although FASD is often not diagnosed until later in life, prenatal and/or postnatal growth retardation can be detected if weight, length, and/or head circumference are below the 10th percentile corrected for gestational age (Department of Health and Human Services 2004). While small HC on its own would not be indicative of FASD, it can be a structural impairment caused by FASD.

Macrocephaly

Macrocephaly is a condition in which HC is significantly larger than average for age and gender. Macrocephaly is present when HC is above the 97th percentile.

Macrocephaly can be characteristic of a variety of disorders, but may also be inherited. Although one form of macrocephaly may be associated with mental retardation, in approximately one-half of cases mental development is normal (National

Institute of Neurological Disorders and Stroke 2013). Macrocephaly may be caused by an enlarged brain or hydrocephalus (fluid on the brain) (Barbier et al. 2013; Kuban et al. 2009; Kurtoglu et al. 2012). It may also be associated with disorders such as dwarfism, neurofibromatosis, and tuberous sclerosis (National Institute of Neurological Disorders and Stroke 2013).

Risk factors and causes

Microcephaly may stem from a variety of causes that lead to the disruption of various stages of brain development. Some causes include genetic abnormalities such as Down syndrome and other chromosomal syndromes, malnutrition, and infections such as rubella or chickenpox during pregnancy. Babies may also be born with microcephaly if, during pregnancy, the mother abused drugs or alcohol, was exposed to certain toxic chemicals, or had untreated phenylketonuria (PKU—a rare inherited disorder which results in elevated levels of the amino acid phenylalanine in the body).

Antenatal exposure to corticosteroids is another risk factor for small HC. Women at risk of pre-term birth before 34 weeks' gestation are routinely given a course of antenatal corticosteroids (ACS) and several studies show that fetuses exposed to multiple courses of antenatal corticosteroids have smaller head circumferences at birth (Abbassi et al. 2000; Murphy et al. 2012; Rodriguez-Pinilla et al. 2006). Whether the potential benefits of this repeated therapy clearly outweigh the risks is yet to be determined in randomized prospective controlled trials.

Dietary factors/nutritional intake can also be associated with reduced HC (Skull et al. 1997). While nutritional intake problems are greater in developing rather than developed countries, one study suggests that the consumption of specific foods during pregnancy (for example, carbohydrate foods containing acrylamide) may be associated with reduced HC (Pedersen et al. 2012). A Cochrane review by Ota and others (2012) also found that antenatal nutritional advice to increase energy and protein intake appears effective in reducing the risk of pre-term birth and increasing head circumference at birth. Further research is needed, however, to assess the effects of increasing energy and protein intake during pregnancy in women whose intake is below recommended levels.

HC also appears to have some relationship with *Autism spectrum disorders* (Schrieken et al. 2013); however, it is not clear how predictive HC at birth is for autism. Some research suggests that children with autism and pervasive developmental disorder have a significantly smaller HC at birth and that their HC then increases disproportionately rapidly in the first year of life (Mraz et al. 2007; Torrey et al. 2004). However, there is also significant general body growth in autistic children in infancy, which suggests that the larger head circumference may be part of excessive general growth (Torrey et al. 2004). The relationship between HC and autism therefore does not appear to be simple or straightforward, except that a smaller HC at birth to 2 weeks has been found to be associated with a greater number of symptoms related to social impairment and autism spectrum disorder (Mraz et al. 2007).

Macrocephaly is often familial or benign, and may not always be associated with a disorder (National Institute of Neurological Disorders and Stroke 2013). The presence of excess fluid in the brain (hydrocephalus) may be a risk factor for macrocephaly, and can indicate a problem with the brain, which may require treatment (National Institute of Neurological Disorders and Stroke 2013).

The view of the National Institute of Neurological Disorders and Stroke (NINDS) is that cephalic conditions or disorders are not necessarily caused by a single factor and may be influenced by hereditary or genetic conditions or by environmental exposures during pregnancy such as medication taken by the mother, maternal infection, or exposure to radiation. Some cephalic disorders occur when the cranial sutures (the fibrous joints that connect the bones of the skull) join prematurely.

Prevalence/incidence, mortality and trends

Due to the way percentiles are calculated, by definition approximately 10% of a population should be <10th percentile (small head circumference), approximately 80% between the 10th and 90th percentiles (normal head circumference), and approximately 10% >90th percentile (large head circumference). Using <3rd and >97th percentiles to define microcephaly and macrocephaly respectively, this would mean that in Australia each year there are approximately 9,000 babies born with microcephaly and 9,000 babies born with macrocephaly. However there is not necessarily a straightforward relationship between percentiles and associated morbidity. Not all babies with microcephaly or macrocephaly will have morbidity associated with the condition.

In some sub-populations, however, the prevalence of microcephaly is high. For example, one international study found the prevalence of microcephaly among children being evaluated in neurodevelopmental clinics ranges from 6% to 40%, with an average prevalence of 25% (Ashwal et al. 2009). Although significant numbers of children with microcephaly carry a risk for low Intelligence Quotient (IQ), the presence of microcephaly itself is not necessarily indicative of intellectual disability. In another study of children with mild microcephaly (defined in this case as between 2–3 standard deviations below the mean), 10.5% had IQ scores below 70 (meeting the definition of intellectual disability), and 28% had borderline scores between 70 and 80 (Dolk 1991).

Data collection and analysis issues

There is debate on how data from growth charts should be interpreted. There can be problems due to inaccurate data, the discontinuous nature of growth, the use of single values, and time intervals between observations (Legler & Rose 1998). For pre-term babies there is the added problem of error in gestational age dating, which affects the accuracy of the size/age relationship represented in growth curves (Olsen et al. 2010). Recommended cut-off values also vary according to the risks infants are being screened for. All of these concerns need to be taken on board when assessing the value of reporting HC percentiles as part of the NPDC.

There is also debate about the number of measurements to be taken. Some researchers indicate that a single measurement can provide some useful information—but multiple measurements are generally preferred. One-time measurements may be used to screen for some risks; however, they do not provide adequate information for determining a growth pattern (Dietitians of Canada and Canadian Paediatric Society 2004). While poor growth may be reflected by an extreme measurement centile on a single occasion (Royal Children's Hospital and Victorian Department of Education and Early Childhood Development 2012), many researchers argue that a single growth percentile value at any particular point is of limited usefulness. Rate of growth is often deemed more important, and children whose growth parameters are at the

extremes of the growth curve but whose growth rates are normal are likely to be healthy. Conversely, accelerated or slowed growth rates are rarely normal and warrant further evaluation (Legler & Rose 1998).

Further, HC may be misleading when used without complementary assessments such as estimation of head–body proportionality and appraisal of cranial sutures. For example, some jurisdictional guidelines in Australia (such as in Queensland) indicate that head circumference needs to be measured when determining IUGR and/or SGA and use the 10th percentile as the cut-off point; however they also require length and weight parameters to be less than the 10th percentile. While these two variables may appear superfluous when dealing with overt brain damage, they become essential, and are possibly the only cue in cases of more subtle brain damage as these children rarely reach HC below 2 standard deviations (Amiel-Tison et al. 2002). Therefore, complementary assessment is considered essential for early identification of children at higher risk of unfavourable long-term outcome.

Some researchers have also recommended that data be systematically updated every 5 to 10 years in view of the fact that fetal growth has been changing over the years for various reasons (Amiel-Tison et al. 2002).

Data development undertaken through the National Maternity Data Development Project

Head circumference has been included on the National Maternity Data Development Project (NMDDP) priority data item list for data development. See *Foundations for enhanced maternity data collection and reporting in Australia: National maternity data development project—Stage 1* (AIHW 2014) for more information on the NMDDP priority data item list). It has since been included on the Perinatal DSS 2016–17, for jurisdictions to collect from 1 July 2016 where feasible. While currently optional for collection, it is expected that head circumference will be included in a future Perinatal National Minimum Data Set (NMDS), making it a mandatory item to collect once all jurisdictions are able to implement the necessary collection processes.

The data development process, which began in 2014, included consultation with a clinical and data reference group (CDRG), the NMDDP Advisory Group and jurisdictional stakeholders.

A national health data standard was developed:

Birth—head circumference, total centimetres NN[N].N (METeOR identifier 568380).

(More information about METeOR, the AIHW's metadata registry, is available on the AIHW website at <http://meteor.aihw.gov.au/content/index.phtml/itemId/181162>).

The data standard is designed to capture head circumference measured at birth, preferably at the same time as birthweight, and recorded at least to the nearest 0.5 cms. After much discussion, it was agreed that measurement at birth was the only measurement that could be realistically captured, particularly as many mothers are discharged from hospital on day 1. The data standard provides advice on measurement and recording.

Five jurisdictions already collect head circumference in their perinatal data collections and report it voluntarily to the National Perinatal Data Collection. Some will need to make minor adjustments to forms and systems to accommodate recording to the nearest 0.5 cms. The other three jurisdictions will need to add the data item to their forms and systems, and have agreed in principle to the data item and its definition.

Importance of national collection of these data items

Head circumference is a useful measure to reflect intrauterine brain development and fetal growth. Collection of head circumference data in all jurisdictions through the NMDS will improve national reporting on fetal growth and development, assisting with the recognition of growth restriction, and, consequently, any associated conditions.

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