New Reference Curves for Head Circumference at Birth, by Gestational Age

WHAT’S KNOWN ON THIS SUBJECT: Head circumference (HC) at birth reflects brain development in utero. However, HC charts used in Canada are either dated, mixed-gender, nonrepresentative of lower gestational ages, or reflective of other populations in the world.

WHAT THIS STUDY ADDS: We developed recent and gender-specific reference curves for HC at birth for singletons of 23 to 41 completed weeks’ gestational age, which included a large number of very prematurely born infants, reflecting the current geotemporal Canadian population and advances in obstetric care.

abstract

BACKGROUND: The measurement of head circumference (HC) at birth reflects intrauterine brain development. HC charts currently used in Canada are either dated, mixed-gender, nonrepresentative of lower gestational ages (GAs), or reflective of other populations.

METHODS: To create both birth weight and HC curves, we combined weight and HC data from the Canadian Neonatal Network (CNN) database (admissions in NICUs across Canada) with McGill’s Obstetrical Neonatal Database (MOND; all births at a tertiary hospital in Montreal, Canada). We included CNN data for GAs of 23 to 34 weeks (2003–2007) and MOND data for GAs of 35 to 41 weeks (1995–2008). Nonsingletons, congenital anomalies, and measurements greater than ±4 SD from the mean were excluded. Distributions of birth weight and HC at each GA were statistically (penalized spline regression) smoothed. Birth weight curves were compared with recent Canadian reference curves and HC curves with historical and/or frequently used curves.

RESULTS: We included 39 896 births (3121 births at <30 weeks’ GA) to generate the curves. Current weight curves were similar to Canadian reference charts for both genders. Weight and HC measurements in boys were higher than in girls. When classified according to recent international references, the proportion of CNN-MOND infants at ≥32 weeks’ GA with HCs <10th percentile was significantly underestimated. When classified according to historical reference curves, a significant number of CNN-MOND infants of all GAs with HCs <10th and >90th percentiles were misclassified.

CONCLUSIONS: We developed recent gender-specific reference curves for HC at birth for singletons at 23 to 41 completed weeks’ GA, which included a large number of very premature infants, reflecting the current geotemporal Canadian population. Pediatrics 2013;131: e1158–e1167

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KEY WORDS

growth charts, fetal growth, microcephaly, macrocephaly, preterm birth, birth weight, head circumference, reference curves, brain growth

ABBREVIATIONS

AHC—appropriate head circumference
CNN—Canadian Neonatal Network database
GA—gestational age (completed weeks)
HC—head circumference
LHC—large head circumference
MOND—McGill Obstetric and Neonatal Database
SHC—small head circumference

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The measurement of head circumference (HC) at birth is part of the initial basic clinical assessment of newborns. HC reflects brain volume and brain development in utero.1,2 Plotted onto reference curves, the HC measurement is indicative of in utero growth of the brain for the child’s gestational age (GA). It is thus a major diagnostic and prognostic marker used to help identify symmetric or asymmetric growth, microcephaly (<2 SDs below the mean or <10th percentile) and macrocephaly (>2 SDs above the mean or >90th percentile), all of which are associated with a number of etiologies that require additional investigation.3,4 It is therefore essential that the clinician be provided with trustworthy and representative reference growth curves. Because of improvement of antenatal and postnatal care, including better assessment of GA, it is important that measurement curves be updated, especially for preterm infants.5 However, despite the clinical importance of HC, few recent growth curves are available in the literature. Indeed, measurements of HC are often not included in birth registries and databases used in cohort studies. Figure 1 shows the main HC curves currently in use in North America. Those by Usher and McLean6 are commonly referenced in Canada despite the fact they were published in 1969 and their small underlying sample size (300 total). The Fenton growth chart7 is more recent and based on a larger sample of 30 000 Australian and 380 000 Swedish (but not North American) infants.8,9 In addition, few infants born before 30 weeks’ gestation were included (only 274 infants), because the larger Swedish data set did not include births before 29 weeks.7,9 More recently, Olsen et al10 published HC intrauterine growth curves based on data of a large number of infants born in 33 US states; however, the Canadian newborn population might differ because prematurity rate and socioeconomic disparities are lower, and universal health care and obstetric coverage prevails.11 The objective of the current study was to create up-to-date HC reference charts that are representative of today’s Canadian neonatal (including very prematurely born) population.

METHODS

We merged weight and HC data from 2 existing birth databases: the database of the Canadian Neonatal Network (CNN) and the McGill Obstetric and Neonatal Database (MOND). The curves presented in the current study were generated with CNN data for births at 23 to 34 weeks’ completed GA and MOND data for births at 35 to 41 weeks’ completed GA.

We first used these databases to generate growth curves for weight and verified that they were consistent with existing reference curves for Canadian newborns.12 We then developed HC curves and compared them with existing reference charts.

Population

The CNN (http://www.canadianneonatalnetwork.org/portal/) was established in 1995 and links researchers from 30 hospitals and 17 universities across Canada. The CNN maintains a database of all infants admitted to affiliate NICUs in Canada, from which we obtained data for patients born between 2003 and 2007. The MOND database includes all children born at a tertiary care university hospital in a major urban center (Royal Victoria Hospital of the McGill University Health Centre, Montreal, Quebec, Canada),
which includes ~3700 births per year. Data collected between January 1995 and June 2006 were obtained for the current study. Data collection was incomplete between April 1, 1997, and March 31, 1998, and these data were therefore excluded. The Royal Victoria Hospital NICU is part of the CNN database.

We included birth weight, HC, and GA for all singletons born between 23+0 and 41+6 weeks' GA, excluding stillbirths and infants with major congenital anomalies. Before plotting the curves, we excluded data on children whose weight or HC measurements were at more than ±4 SD from the mean.

In accordance with recommendations by the World Health Organization, we truncated GAs to completed weeks.13 In the MOND database, 89.7% of mothers of neonates born from 1995 to 2006 had their GA validated with ultrasound evaluation; although this information was not directly available from the CNN database, the health care system and rate of antenatal ultrasound use for the Canadian population in recent years were considered very similar. We therefore assumed that the majority of GAs of infants included in this study were accurate.

**Data Selection: Validation With Birth Weight Curves**

We first constructed growth curves for birth weight by GA for each database (MOND and CNN) separately and compared them with the curves for birth weight by GA developed by Kramer et al.12 These curves were selected because they were both recent and representative of the Canadian population, were based on live birth registries across Canada (except for Ontario), and included the largest Canadian sample of low-GA births. The CNN-derived birth weight charts for males and females were very similar to Kramer et al’s12 curves for GAs of 23 to 34 weeks (CNN—Kramer et al’s maximum difference for both genders is —66 g at the 10th percentile of 34 weeks for boys, —39 g at the 50th percentile of 30 and 31 weeks for girls, and —41 g at the 90th percentile of 29 weeks for girls; Supplemental Table 2). However, at higher GAs, although the 50th percentile (median) is comparable, the charts diverged at the 10th and 90th percentiles (CNN—Kramer et al’s curve at the 10th percentile yielded a difference of up to —298 g for boys at 37 weeks and —559 g for girls at 37 weeks and at the 90th percentile yielded a difference of up to +219 g for boys at 38 weeks and +259 g for girls at 38 weeks [Supplemental Table 2]). Differences could be explained by the small numbers and the likely pathologic term and near-term births admitted to NICUs and therefore included in the CNN database. In contrast, the MOND-derived curves were divergent from Kramer et al’s weight curves at ages <35 weeks, whereas at GAs ≥35 weeks, differences were consistently smaller for both boys and girls at the 10th, 50th, and 90th percentiles (maximum difference of 84 g for 10th percentile girls at 41 weeks [Supplemental Table 3]). Therefore, to build the HC reference curves, we elected to use the CNN database for births at 23 to 34 weeks’ GA and the MOND database for births at 35 to 41 weeks’ gestation. Of note, infants in the MOND (ie, from the Royal Victoria Hospital) database who were born at <35 weeks’ GA and admitted to the NICU were included in the CNN database.

**Statistical Analysis**

Penalized spline regression was used to generate smoothed percentiles12 for HC and birth weight. The means and the SDs were weighted by the square root of the number of infants at each GA. The percentiles of the HC and the birth weight distributions were generated by the smoothing spline from the fitted generalized additive models. Data were separated by gender, and tables and charts created for the 3rd, 10th, 50th, 90th, and 97th percentiles. Curves were drawn by using R software version 2.9.0 (http://www.r-project.org). Developed by the Statistics Department, University of Auckland, Australia; available at http://cran.r-project.org/, and the gam() function was used http://cran.r-project.org/web/packages/gam/gam.pdf). Means and SDs were calculated from empirical distribution of HC values and were also tabulated to allow calculation of z scores.12

The new CNN-MOND HC curves were compared with the Lubchenco et al,14 Usher and McLean,6 Fenton,7 and Olsen et al10 curves for HC. The CNN-MOND HC data were classified according to the <10th, 10th to 90th, and >90th percentiles of the Lubchenco et al,14 Fenton,7 and Olsen et al10 curves, and according to the means ±2 SDs of the Usher and McLean6 curve. The proportion of misclassification was calculated for GAs stratified as 23 to 26 weeks, 27 to 31 weeks, 32 to 36 weeks, and 37 to 41 weeks, and a likelihood ratio χ2 was calculated to assess statistical differences.10

**RESULTS**

**Population**

From 2003 to 2007, data for 26 482 infants born between 23+0 to 34+6 weeks GA were collected in the CNN database. In the MOND database, 35 519 infants were born from 1995 to 2006 (excluding April 1997 to March 1998) between 35+0 and 41+6 weeks GA. Of those, 18 675 in CNN and 32 749 in MOND had both birth weight and HC recorded. After exclusion of nonsingletons, those with congenital anomalies, and infants with HC or birth weight values more than ±4 SDs from the mean for GA, the final sample included 10 272 infants <35 weeks’ GA.
Data Selection: Validation With Birth Weight Curves

The birth weight curves at the 10th, 50th, and 90th percentiles obtained from our combined CNN-MOND data showed a high degree of observable similarity to the most recent Canadian gender- and GA-specific fetal growth standards, both for boys and girls (Fig 3 A and B). When CNN-MOND data were separated as <10th, 10th to 90th, and >90th percentiles and compared with the Kramer et al curve, the differences were small overall (see Supplemental Tables 2 and 3).

HC Curves

We then calculated average HC values at GAs of 23 to 41 weeks and at the 3rd, 5th, 10th, 50th, 90th, and 97th percentiles, including both the median and the mean ± SD (Table 1). The smoothed curves closely followed (within limits of random error) the empirical HC distribution at each GA. For example, at 35 weeks, the 90th percentile curve excludes 90.5% of males and 92.1% of females in our data set. At 40 weeks, the 10th percentile curve excludes 9.2% of males and 11.7% of females. Figure 4 shows the curves (raw and smoothed) for HC at birth, as obtained from our merged CNN-MOND data. Supplemental Table 4 shows the differences between our values and those obtained from previously published reference curves.

Comparison With Lubchenco et al (Denver, Colorado; 1948–1961)

Although Lubchenco et al’s HC growth curve starts at 26 weeks’ GA and is not gender-specific, it is still used in many NICUs. CNN-MOND current HC curves (including 3121 births at GAs of <30 weeks [1688 boys, 1453 girls] and 2374 infants at GAs of ≤28 weeks [1252 boys, 1122 girls]) and 29,624 infants ≥35 weeks’ GA (Fig 2).

FIGURE 2
Study population. BW, birth weight.
for boys and girls versus the unisex Lubchenco et al curves are presented in Supplemental Fig 6 A and B. The classification of current reference curves using the Lubchenco et al curves (Supplemental Table 5) showed a significant proportion of GAs ≥32 weeks with a small HC (SHC) and of GAs ≤36 weeks with a large HCs (LHC) classified as having an appropriate HC (AHC) for GA (32% to 87% misclassification). For 38 weeks of gestation and older, Lubchenco et al’s 50th percentile tended toward the CNN-MOND 10th percentile (Supplemental Fig 6 A and B).

Comparison With Usher and McLean (Montreal, Canada; 1959–1963)

The unisex Usher and McLean curves were generated from 300 infants born in 1959 to 1963. A comparison of birth weight CNN-MOND curves versus Usher and McLean curves are presented in Supplemental Fig 7 A (boys) and B (girls). With regard to HC, differences between these unisex curves were present for boys mainly for values at +2 SDs from the mean, where current measures were higher than Usher and McLean’s throughout GAs (Supplemental Fig 8A). In girls, the HC curves were similar; except our −2 SD values were lower, particularly at GAs of ≥37 weeks (differences ranged between 0.6 and 0.7 cm) (Supplemental Fig 8B). The classification of current references using the Usher and McLean curves (Supplemental Table 6) shows a significant proportion of all SHC and LHC infants present for boys and girls versus the unisex Lubchenco et al curves are presented in Supplemental Fig 6 A and B. The classification of current reference curves using the Lubchenco et al curves (Supplemental Table 5) showed a significant proportion of GAs ≥32 weeks with a small HC (SHC) and of GAs ≤36 weeks with a large HCs (LHC) classified as having an appropriate HC (AHC) for GA (32% to 87% misclassification). For 38 weeks of gestation and older, Lubchenco et al’s 50th percentile tended toward the CNN-MOND 10th percentile (Supplemental Fig 6 A and B).

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classified as AHC (26% to 74% misclassification).

Comparison With Blidner et al (Hamilton, Canada; 1974–1975)

Blidner et al's\(^{15}\) growth curves were developed from a random sampling of 1231 infants in Ontario, Canada, in 1974 to 1975, and present unisex HC values for GAs of \(\geq 31\) weeks and gender-specific values for GAs \(\geq 36\) weeks. Our proposed reference matches closely with Blidner et al's, with differences of \(\leq 0.5\) cm at all percentiles for boys and girls (Supplemental Table 4).

Comparison With Fenton (Sweden, Australia; 1977–1995)

In 2003 Fenton\(^{7}\) published practical growth curves that assembled on 1 sheet Canadian birth weight curves (from Kramer et al\(^{12}\)) and HC curves generated by combining Swedish and Australian databases. Comparisons of current HC curves with Fenton's are presented in Fig 5 A (boys) and B (girls). Current HC values for boys at the 90th percentile were higher overall (Supplemental Table 4). This finding was particularly apparent at GAs of 23 to 28 and 33 to 37 weeks (differences ranged between 0.6 and 1.3 cm). At the 50th percentile (median), our proposed reference was closer but still higher than Fenton's (differences ranged between 0.5 and 0.9 cm at weeks 33–38).

**FIGURE 4**
Reference curves for HC at birth by GA for Canadian singletons. Curves were obtained from combined CNN-MOND data, as crude data and after smoothing. For all of the panels, the 3rd, 10th, 50th, 90th, and 97th percentiles are presented. A, HC (crude data) at birth for boys at 23–41 weeks' GA. B, HC (smoothed) at birth for boys at 23–41 weeks' GA. C, HC (crude data) at birth for girls at 23–41 weeks' GA. D, HC (smoothed) at birth for girls at 23–41 weeks' GA.
and tended to converge at 39 weeks. At the 10th percentile, current values were higher from 33 weeks and older (differences ranged between 0.6 and 1.1 cm). For girls (Supplemental Table 4), our and Fenton’s curves were similar (differences <0.5 cm), except that our 10th percentile values were lower at GAs <28 weeks (differences estimated on the published curves ranged between 0.7 and 0.8 cm). The classification of current reference using the Fenton curves (Supplemental Table 6) showed a significant proportion of 32 to 36 and 37 to 41 GA weeks SHC and of 37 to 41 GA weeks LHC infants classified as AHC (26% to 41% misclassification).

Comparison With Olsen et al (Multiple Sites, United States; 1998–2006)

Two trends emerged when we compared current curves with Olsen et al10 (Fig 5). For both genders, HC values were consistently higher than Olsen et al’s at the 90th percentile (differences ranged between 0.6 and 1.4 cm) for GAs younger than ~31 weeks (Supplemental Table 4). The 50th percentile of current curves and Olsen et al’s curves overlapped. For the 10th percentile, current HC measures were higher for GAs >32 weeks (differences ranged between 0.5 and 1 cm). The classification of current references using the Olsen et al curves (Supplemental Table 6) showed a significant proportion of 32 to 36 (41%) and 37 to 41 (66%) GA weeks SHC infants misclassified as AHC.

DISCUSSION

We have produced a set of new, up-to-date reference curves for HC at birth that were based on a large Canadian population, are gender-specific, and are valid for births between 23 and 41 weeks’ gestation. Overall, measures in boys were higher than in girls. We also note that Canadian newborn HCs at the 10th and 90th percentiles differed from recent North American US references.

For the development of these curves, we merged 2 complementary databases to achieve a good sample size of both preterm and term neonates: the CNN database, which comprises most of the NICUs in Canada, and the MOND database of a tertiary care maternity hospital in a large urban center (Montreal, Quebec, Canada). We verified our methodology by plotting birth weight curves on the basis of our combined data and comparing them with the reference charts of Kramer et al,12 which were based on a 1994 to 1996 Canadian (except for Ontario) population study. We then generated HC curves and compared them with existing charts with specific attributes: historic (Lubchenco et al,14 Usher and McLean,6 and Blidner et al15), frequently used (Fenton7), and recent (Olsen et al10).

One particular advantage of our reference curves is that they were based on the population of a single country that is relatively affluent and with free access to prenatal care. The importance of a geographical link between optimal birth weight and lowest perinatal and neonatal mortality was revealed by the EuroNatal Working Group.16 The same would be expected to hold true for HC. The second advantage is that our data for preterm births under 35 weeks’ gestation dated from 2003 to 2007, which was recent enough to reflect some of the latest advances in the rapidly changing field of perinatology17 and can be related to the recent birth weight curves. The third advantage is the better GA assessment of the current cohort compared with those of historical curves.
Another major strength of our HC reference curves is the large number of very preterm births included in the database, which was an order of magnitude greater than that of any other HC curve based on a Canadian population (Fig 1). Of the other HC curves currently in use in Canada, those of Fenton7 were based on a non-Canadian population and those of Olsen et al10 on a US population. Our large sample allowed for the segregation of preterm births by gender, a major determinant of fetal growth.18,19

Except for Blidner et al15 at the higher GAs (with which our values matched well) and Olsen et al,10 none of the other curves were gender-specific. The reference curves proposed by the current study indeed showed higher measures of HC's in boys versus girls, as also observed for birth weight. Overall, when comparing our HC curves with recent others, we noted 2 major trends, both of which were seen more particularly in boys: a consistent upward shift in the 90th percentile at most GAs and an overall upward shift at the 10th percentile starting at 34 weeks. When classifying current data according to <10th, 10th to 90th, and >90th percentiles of other published curves, a significant understimation of infants with HC's <10th percentile was particularly present with all comparison curves, both historical6,14 and more recent.7,10

It has been suggested that birth weight has been steadily increasing in developed countries, including in the Canadian population.20,21 Current CNN-MOND birth weight curves differed little from the previous Canadian reference curves that date from the mid-1990s; this finding could be due to a “slowing” of increasing birth weights in newborns or to the fact that not enough years separated the 2 study periods to unravel differences (MOND data used for the current study and Kramer et al12 data overlap for the years 1995–1996). Increases in birth weight could reflect increases in average weight and incidence of overweight in the population, rather than “improved” overall fetal growth and health resulting from improved life habits (less smoking) and improved prenatal obstetric care: HC data, in addition to birth length, would be essential to study these possibilities. However, birth lengths and HC are not variables currently collected in most administrative birth registries. Indeed, most recent Canadian neonatal anthropometric curves concerned only birth weight.12,22 Length data in newborns are a measure with high interobserver variability if not realized with the use of a well-calibrated and reproducible procedure; however, HC has a lower inter- and intraobserver variability.23,24

HC curves, like weight curves, can be based on longitudinal or cross-sectional measurements. Intrauterine growth charts (based on measurements made by ultrasound examination either cross-sectionally or longitudinally) represent the whole population of healthy pregnancies as well as those at risk of premature delivery.25 Nevertheless, ultrasound assessments remain less precise than direct measures taken on the infant; and growth charts based on measures taken at birth (ie, cross-sectional) of infants of all GAs remain an important reference for clinicians in the evaluation of size for GA at birth. For preterm infants, however, these curves do not well represent, by definition, growth through a normal pregnancy because a preterm delivery may reflect an underlying pathologic pregnancy. Preterm infants are more likely to suffer from intrauterine growth restriction or other health issues compared with fetuses who remained in utero.26–28 Despite these limitations, growth charts based on direct measures taken at birth, such as the ones produced in the current study, are used in most NICUs to assess size at birth as well as to monitor growth up to term.

The identification of infants with SHC for GA is an important element for the complete assessment of a newborn and for the determination of specific investigations as well as medical and neurodevelopmental follow-up requirements. With the historical and the more recent curves, a number of newborns in the current cohort would be classified with an appropriately grown HC when in fact it is below the 10th percentile, and would therefore not be identified for additional medical attention.

One limitation of our study stemmed from the fact that the MOND database (data for the 35–41 weeks) was single site. However, this limitation was offset by the sheer number of patients in the database (close to 30,000 after exclusions), the multiethnic nature of the Montreal population, and by comparing birth weight for the GAs taken from MOND with data published by Kramer et al.12 Another limitation came from the fact that the CNN was based on neonates who were admitted to NICUs and that therefore a selection bias could be suspected. Indeed, this database did not include stillbirths and deaths in the delivery room, but these represent a very small proportion of newborns. Some late preterm infants (33–34 weeks) might not be automatically admitted in all of the NICUs; however, the comparison of the birth weight in Kramer et al’s population-based curves revealed that this bias was unlikely.

CONCLUSIONS

The current study presents recent and gender-specific HC curves. These Canadian newborn HC's showed some differences compared with recent North American US references. To accurately
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New Reference Curves for Head Circumference at Birth, by Gestational Age
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