LENGTH AND HEAD CIRCUMFERENCE AT BIRTH: ASSOCIATIONS WITH BIRTH OUTCOME AND MORBIDITY IN MACROSOMIC FINNISH INFANTS

Jenni Vaarno
Master's thesis
Public Health Nutrition
School of Medicine
Faculty of Health Sciences
University of Eastern Finland
September 2014

UNIVERSITY OF EASTERN FINLAND, Faculty of Health Sciences
Public Health Nutrition
VAARNO, JENNI: Length and head circumference at birth: associations with birth outcome and morbidity in macrosomic Finnish infants.
Master's thesis, 65 pages.
Instructors: Arja Erkkilä, PhD & Docent and Hanna Lagström, PhD & Docent
October 2014

Keywords: birth weight, length and head circumference, macrosomia, adverse birth outcome

Size at birth is important determinant of birth outcome and perinatal mortality and morbidity. Being too big at birth puts the newborn at increased risk of various health problems at or after birth. The aims of this study were to estimate the prevalence of large birth weight and adverse maternal and infant health conditions related to large birth weight and to determine the effects of newborn body size measured with birth length and head circumference on these health conditions in macrosomic (birth weight >4000g) newborn. Various birth outcomes for both newborn and mother were used. Data for this study was from the National Birth Register from 2008 to 2010 from Southwestern Finland. Only singleton, live births and term pregnancies were included to the analysis (n=10006) and fetal anomalies were excluded. Eighteen percent of the newborns had birth weight over 4000g and thus defined as macrosomic, 2.6% had birth weight above 4500g. Macrosomia was associated with prolonged labor, unplanned cesarean section, postpartum hemorrhage, perineal trauma, the use of medical pain relief, duration of hospital stay, shoulder dystocia, hypoglycemia, low Apgar score and treatment or monitoring at the hospital. The prevalence of prolonged labor, caesarean section, hospital stay, shoulder dystocia, hypoglycemia, low Apgar score at 1 minutes and being treated and monitored at the hospital increased as birth length increased. Increasing head circumference was associated with increasing prevalence of prolonged labor at 2nd stage, caesarean section, hospital stay of the mother and perinatal asphyxia. In conclusion birth length and head circumference were associated with many birth outcome variables in macrosomic infants, usually linked in literature often only with high birth weight. The result suggests length and head circumference would be valuable additional predictors with birth weight, when evaluating perinatal morbidity risk.

Contents

1 INTRODUCTION

Human embryo goes through tremendous alteration during pregnancy from tiny zygote to full developed infant in just nine months. After being born, infants' size is measured to evaluate retrospectively growth in prenatal period and intrauterine environment, but size at birth has also implications for long-time growth and development, mortality and morbidity. Measuring size at birth is important for monitoring of individuals growth and development and for public health in efforts to improve neonatal and maternal morbidity and mortality.

Size at birth can be estimated with multiple anthropometric parameters, depending on measuring equipment available in the situation. Each parameter has different implications to infants' health and wellbeing. The most used parameter of size at birth globally is birth weight, which is easy and precisely measurable, weight scales being available commonly in health facilities in most parts of the world. Birth length, head circumference are used less globally, but in most developed countries. Chest circumference, mid-upper arm circumference (MUAC) and abdominal circumference can be used as substitutes for weight measuring if scales are not available. Combining anthropometric parameters with information about gestational age provides more reliable method for evaluating growth and development of newborn. However, in many developing societies gestational age cannot be accurately determined.

The average size differs between populations depending upon intricate combination of genetic and environmental factors and is continuously in transition stage. In better of societies environmental conditions favor fetal growth and size at birth is on average bigger than in developing societies. However there has not been historically very large variation in anthropometric parameters. Average birth weight varies globally between 3200 to 3700 grams; birth length is close to 50 centimeters and head circumference close to 35 centimeters. Lack of reliable and comprehensive data, especially from developing world hinders the comparison of size at birth globally.

Infant attains optimal size at birth if fetal intrinsic or maternal or uteroplacental extrinsic factors allow fetus to grow according to her/his genetic potential and if space of time spent in uterus is optimal for the development. Fetuses' genetic or chromosomal abnormalities or infections, mothers' diseases, substance use, parity or inappropriate nutrition or malfunctioning uterus or placenta may have an impact on fetal growth or gestational age and thus affect infants' size at birth. The exact optimal size at birth has not been determined, since there is always variation in size at birth due to genetic background and environmental conditions. However many different classification systems are at use to classify infants' size as optimal, small or large.

Size at birth has been associated with various health outcomes in short and long term. Small size at birth, usually measured by birth weight, has been associated with adverse birth outcome, death and increased risk for later morbidity. Also associations between large size at birth and morbidity and mortality have been found in many studies. It is not known, whether size at birth directly causes these adverse health consequences or whether mortality and morbidity are caused by some other factors that cause also size at birth deviate from optimal. However, anthropometric measurements provide important information and are well grounded indicators for health and wellbeing.

2 THEORETHICAL BACKGROUND

2.1 Measuring the size at birth

Size at birth is an important predictor of health and therefore should be measured as accurately as possible for planning and implementation of infant care accordingly. Accurate and reliable monitoring of infant size is especially important for infants at risk for inadequate growth or other health conditions. Size is estimated also during pregnancy to possibly detect possible abnormalities in growth, but exact measurements can be obtained just after birth. There are several anthropometric measurements used to evaluate newborn size at birth; birth weight, birth length, head circumference, chest circumference, mid-upper arm circumference (MUAC) and abdominal circumference. Of the above-mentioned, birth weight, length and head circumference are most commonly used globally and chest circumference, MUAC and abdominal circumference are used ordinarily as a surrogate measurement, if weight scale or length board are not available (WHO 1993).

2.1.1 Birth weight

Birth weight is measured with a baby scale where newborn is lying down in the weighting pan (Salo, Mäki & Dunkel, 2011). Scales used in Finland are nowadays electronic, but in many countries also mechanical baby scales may be used. Newborn is measured nude to prevent error caused by clothes in the measurement. Other anthropometric measurements performed after birth (length and head circumference) are taken meanwhile weight measurement. Weights of the children were measured to the nearest 0.01 kg. Measurement can be performed by one person, since baby can lie freely in the weighting pan.

2.1.2 Birth length

Newborn length should be measured in the recumbent position with calibrated lenghtboard, which has a fixed headpiece, moveable foot piece and well readable measurement tape on the surface of board (Salo, Mäki, Dunkel 2011). Newborn length is measured from top of the head to heels. Infant is positioned straight on his/her back in the center of the board head touching the headpiece and eyes looking straight up. Both legs should be extended and toes should be pointing upwards and feet flatly against foot piece. Two persons are needed for measurement, one holds infants head on a headpiece and the other holds legs straight, moves the foot piece to touch feet and reads the measurement result. Measurements are done to the nearest millimeter.

2.1.3 Head circumference

Head circumference must be measured with flexible, non-stretchable measuring tape (Lönnqvist, Mäki & Salo, 2011). Measurement tape can be made from plastic or metal and it is needed to be changed every half year. Head circumference or occipital frontal circumference is measured over the largest circumference of the head, above eyes and ears. Child is lying down when measured. Measurement tape is positioned just above ears and eyebrows and around the biggest part of the back of the head. It should be assured that tape is straight and it is pulled affectionately to compress hair and soft tissues. Measurement is read to the nearest 0,1cm.

2.1.4 Other measurements

Measurements of chest circumference, MUAC and abdominal circumference are done when newborn is lying down without clothing. To measure chest circumference measuring tape is placed under newborn’s chest at the nipple line (Basavanthappa 2006, Walraven et al. 1994). MUAC is measured from mid-point of left arm, when arm is straightened (LabSpace 2013, Sauerborn et al. 1990). Tape needs to be positioned to skin with proper tension, without making any crinkle to the skin, but also not having any crack between skin and tape. MUAC can be measured with normal measuring tape, or there are special tapes available from organizations working with malnutrition designed only to measure MUAC. Abdominal circumference is measured by placing the measuring tape around infant’s abdomen to a level of navel (Basavanthappa 2006). Tape is placed around abdomen firmly, but not too tightly.

2.2 Terms and definitions related to size at birth

Most commonly used measurements are based on birth weight and there are concepts related to weight only or taking gestational age in the consideration. Body mass index (BMI) commonly used in adults is not used in newborn children. Growth in fetal period has long been known to be associated with sex of the child, multiplicity and gestational age (Stein and Susser, 1984). Using definitions based only on anthropometric measurements, mainly weight, to classify newborn too small or too large may result in misclassification of small or large newborns for their race, gender and gestational age. Thus population and gender specific centile charts have been developed in many countries, including Finland, for classifying infants according to gender as small, normal or large for gestational age. In Finland standards for intrauterine growth developed by Pihkala and coworkers have been used for classifying newborns according to their gender and gestational age for over twenty years (Pihkala et al. 1989). New intrauterine growth charts for weight, length and head circumference has been published in 2013, based on data of 750 000 infants born in Espoo in 1983 - 2009 (Sankilampi et al. 2013).

2.2.1 Low birth weight

Low birth weight (LBW) is defined by the World Health Organization (WHO) as birth weight less than 2500 grams (UNICEF & WHO, 2004). Very low birth weight (VLBW) is birth weight less than 1500 grams and extremely low birth weight (ELBW) less than 1000 grams.

2.2.2 High birth weight and macrosomia

High birth weight (HBW) is defined as birth weight values above 4000 grams and above 4500 grams as exceptionally high birth weight (ICD-10 1999 & 2010). Other term used for high birth weight is macrosomia, but should the criterion of macrosomia be 4000 grams or 4500 grams, is still debatable and both criterions are used (Chatfield 2001, Teramo 1998). In a study made in the USA, birth weight exceeding 4000 grams was already associated with maternal and fetal complications, but in infants with birth weight over 4500 grams morbidity was significantly more prevalent and it was suggested to be a better indicator of infant morbidity (Boulet, Alexander, Salihu 2003). Also the high amount of infants with birth weight over 4000 grams favours using higher criteria level for macrosomia (Teramo 1998). Body mass index (BMI) used in adults to classify overweight and obesity is not used usually in newborn.

2.2.3 Ponderal index

A measure of ponderal index (PI) was developed by Rohrer in 1921 and can be calculated with following formula (Rosso 1989):

$$PI = \text{Birth weight} \times 100 / \text{Length}^3$$

PI can be used to evaluate prenatal growth and infant's body proportionality and it does not take gestational age in to consideration. PI is low when newborn has low soft tissue mass and is thin and high in obese newborns. PI has also been used to describe intrauterine growth retardation (IUGR) or macrosomia (Djelmis et al. 1998, Fay et al. 1991, Vintzileos et al. 1986). Miller and Hassainein published standard curves of PI for gestational age and according to their study normal (10th – 90th percentile) PI was between 2.3 – 2.85 g/cm^3 (Miller & Hassainein 1971). PI used with size of birth for gestational age is a reliable measure of neonatal and adult morbidity. However, PI is based on slower increase of length compared to weight if fetus experiences malnutrition, which might not be the case with chronic malnutrition, when both weight and height are affected (Mehta et al. 1998).

2.2.4 Gestational age

Gestational age (GA) is the time between the first day of the last menstrual period and the day of the delivery (AAP 2004). The first day of last period has been widely used in determining GA and expected date of delivery, because the exact day for conception is usually unknown. Method is quite reliable as long as menstrual dates are remembered accurately. However, irregular menstrual cycles or bleeding during conception may hamper estimations. Assessment of GA can also be done with ultrasound examination performed before 20th gestational week, ideally at eight to 13 weeks of gestation (Peleg, Kennedy & Hunter 1998). Later in pregnancy ultrasound is not that reliable and should not be used. GA is reported as weeks.

Yehuda Malul’s image illustrates different terms and definitions related to birth weight (Figure 1, Yehuda, 2013). As can be seen from the figure, low birth weight, very low birth weight and extremely low birth weight are used, when birth weight is lower than set limit despite of gestational age. Another measure based on only birth weight; high birth weight is absent from the picture. When definitions of small for gestational age (SGA), appropriate for gestational age (AGA) and large for gestational age (LGA) are used, also gestational age is taken into consideration. Different definitions can overlap; for example LBW infant can be at the same time also defined as AGA or LGA or normal weight infant can be defined as SGA. In the figure SGA, AGA and LGA newborn are classified based on percentiles, but also standard deviations can be uses; for example appropriate for gestational age or AGA can be classified also as -2SD to +2SD for weight (Sankilampi et al. 2013).

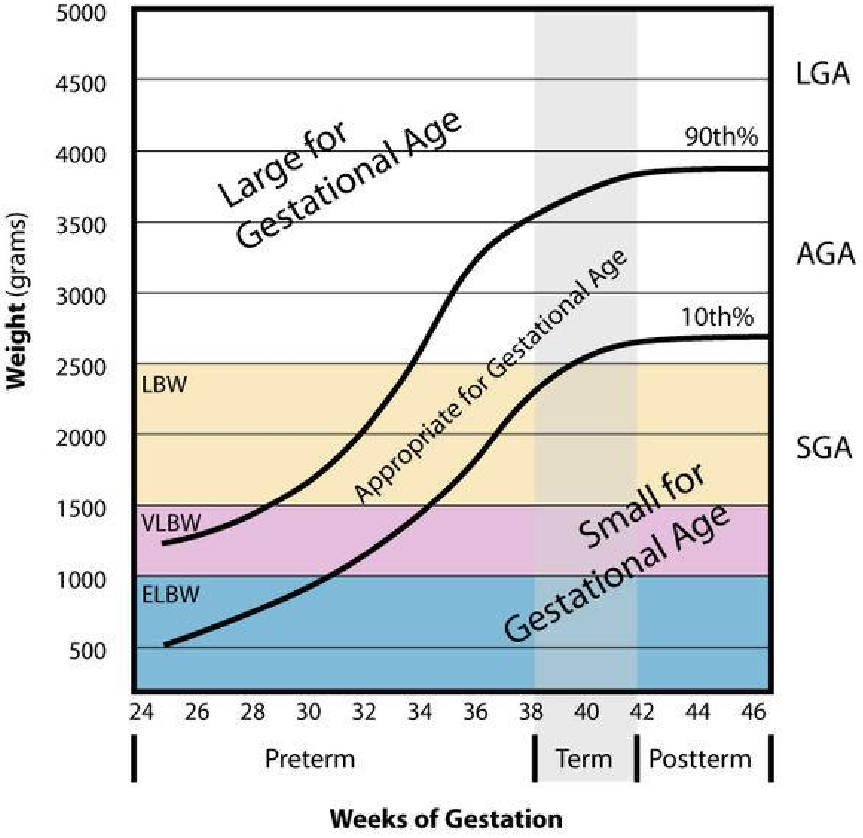

Figure 1. Terms and definitions related to birth weight. LBW = low birth weight, VLBW = very low birth weight, ELBW = extremely low birth weight, LGA = large for gestational age, AGA = appropriate for gestational age and SGA = small for gestational age (Yehuda 2013).

2.2.5 *Small for gestational age and intrauterine growth restriction*

The term small for gestational age (SGA) is used for newborns with estimated weight, length or weight and length being less than -2SD's for gestational age (ICD-10 1999). Symmetric growth failure is defined as both length and weight being abnormal and asymmetric when weight is less than – 2SDs and length is normal. Also size being less than 10th percentile in growth curves is used to classify child as SGA (Olsen et al. 2010). The use of SDs or percentiles in defining SGA requires accurate estimation on the gestational age and may be unfeasible in many developing countries due to lack of contemporary obstetrics resources. In these countries measures based only on birth weight are used more often to identify abnormal growth.

SGA children may be preterm, term or post-term and also etiology of growth restriction differs (Itani, Niedbala & Tsang 2005). SGA children can be divided roughly to three classes according to origin of the growth restriction (Wennegren 1992, Peleg, Kennedy & Hunter, 1998):

1) Children who are well nourished and healthy, but grow according to their genetic potential to be smaller than most of the newborns.

2) Children who are SGA because of chromosome disorders or infections during prenatal period. For example trisomias, Turner's syndrome or cytomegalovirus, herpes, rubella or toxoplasmosis infections may cause SGA.

3) Children whose growth has decelerated due to placental malfunction. This can be due to placental insufficiency because of elevated α-fetoprotein levels or preeclampsia or placenta may be abnormal due to abruption of placenta, placenta previa, infarction or hemangioma.

The last two occurs when fetus does not grow according to her/his growth potential due to reasons mentioned above and can be called also intrauterine growth restriction (IUGR) (Dunkel 2010, Peleg, Kennedy & Hunter 1998). Innately small infants have usually symmetric body and develop normally, but growth-restricted infants can be malnourished or dysmorphic. IUGR and SGA do not always exist always simultaneously; also growth-restricted infants can have appropriate size for gestational age. In study by Marconi et al. (2008), 53 percent of growth-restricted infants were also SGA and rest had an appropriate weight for gestational age. Other study estimated that approximately 30 percent of SGAs have also had IUGR (Ott 1988).

2.2.6 Large for gestational age

Large for gestational age (LGA) stands for newborns with estimated weight being more than +2SD's for gestational age (ICD-10 1999). LGA is also defined as birthweight larger than

90th percentile for gestational age (Weissmann-Brenner et al. 2012). Also term macrosomia has sometimes been used about large babies for gestational age. LGA infants differ on their phenotype and metabolics, which is assumed to be due symmetry of the body (Lepercq et al. 1999). Asymmetric LGA with high weight and low length could be more detrimental than symmetric LGA and therefore it was suggested that classification would not be based only on birth weight and gestational age.

2.3 Contemporary size at birth

For monitoring of size at birth it is important to consider, that globally large proportion of infants are not measured at birth or recorded and even if birth weight is measured, birth length or head circumference are measured seldom. It has been estimated, that in developing countries over half (58 percent) of the infants are not weighed, varying from 17 percent in Latin America and Caribbean to 74 percent in South Asia (UNICEF & WHO 2004). Defective measuring of size at birth hinders at individual level later monitoring of child’s growth and estimating standard growth on a population level.

2.3.1 Birth weight

No instance monitors birth weight globally. Good estimates of birth weight from developing world are received from Demographic and health surveys (DHS) (Measure DHS, 2013). In the survey respondents are asked, whether there have been live births in the last three years preceding the survey, if child’s weight has been measured and what has been the birth weight of the child. Birth weight is recorded in DHS’s as birth weight’s less than 2.5 kg or more than 2.5 kg. Measure DHS has a database STATcompiler, where data on DHS surveys can be obtained as tables or figures (http://www.statcompiler.com/). Lowest prevalence of normal birth weight in developing countries is in Sub-Saharan Africa and highest in South America, South East Asia and Central Asia.

In seven European countries, the modal birth weight varied between 3384 grams in Flanders, Belgium to 3628 grams in Finland (Graafmans et al. 2002). In Portugal, the average birth weight was 3276 grams among Portuguese children and 3284 grams among African children in 2002 (Harding et al. 2006).

Of all the births in the world, low birth weight babies represent 15.5 percent, of which 95.6 percent of them in the developing world (UNICEF & WHO, 2004). However these figures are just estimates and the actual proportion of LBW babies is estimated to be larger. Highest prevalence of low birth weight infants can be found from South-central Asia; 27 percent. In the USA, prevalence of SGAs was 8.6% (Hediger et al. 1998). In OECD countries the average prevalence of LBW was 6.5 percent being highest in Turkey (11.3 percent) and lowest in Iceland (3.5 percent) (OECD 2009). Reliable figures on prevalence of SGA in developing world are difficult to obtain due to inaccurate determination of gestational age, but prevalence is estimated to be approximately 30 million newborns per year (de Onis, Blössner & Villar 1998). In recent Lancet series on maternal and child undernutrition IUGR was defined as newborns born estimatedly at term with a low birth weight (< 2500 grams) (Black et al. 2008). Prevalence of these newborns was 10.8 percent in all developing countries, being lowest (4.9 percent) in South America and highest (19.9 percent) in South-central Asia.

Prevalence of macrosomia varies in different countries between 5 to 20 percent (Henriksen 2008). In developing countries prevalence of macrosomia is still low compared to developed countries. However, prevalence is expected to continue rising due to diabetes and obesity among women in reproductive age also in the developing world (Koynagi et al. 2013). In the USA, 10.5 percent of infants were LGA (Hediger et al. 1998).

The average birth weight in Finland was 3515 grams in singleton births, 2494 grams in twin births and 1616 grams in triplet births in 2009-2010 (Vuori & Gissler 2011). Girls weighed on average 3427 grams and boys 3540 grams and the average birth weight was largest in South Ostrobothnia and the smallest in South Carelia, but the areal differences were small. Four and half percent had birth weight less than 2500 grams, of which 9 percent of infants had birth weight between 1000 to 1499 grams and 9 percent below 1000 grams. SGA infants accounted for 2.2 percent of infants. The percentage of Finnish infants, with a birth weight exceeding 4000 grams was 16.7 and with a birth weight exceeding 4500 grams 2.5 percent in year 2010. The proportion of infants with birth weight over 4000 grams has decreased in twenty years over four percentages, which is suggested to be accounted for improved monitoring of blood glucose levels of pregnant women and concentrated treatment of gestational diabetes to university hospitals. Same proportion (2.5 percent) of infants were LGA, than infants weighting over 4500 grams.

2.3.2 Birth length

Data on birth length are available only from few countries, since it is not measured or recorded in many countries. In the United States new intrauterine curves for size at birth were published in 2010 based on data on 391681 infants in years 1998 to 2006 (Olsen et al. 2010). According to the data the mean birth length of infants born at term (37 to 41 weeks) was 49.9 cm for girls and 50.6 cm for boys. In India mean length of boys at 38 weeks was 49.1 cm for boys and 48.6 cm for girls (Kandraju et al. 2012). In Brasilian sample of 4452 infants, in 28 percent of the infants birth length was 47 - 48.9 cm and in 38 percent 49 – 50 cm and 19.3 percent were over 51 cm tall (Araújo et al. 2008).

The average length of newborns in Finland was 50.0 cm in 2009-2010 (Vuori and Gissler 2011). Boys were taller (50.4 cm) at birth than girls (49.6 cm). There was slight variation in birth length between hospital districts from 49.6 cm in West Pohja, Central Ostrobothnia, South Karelia and North Karelia to 50.1 cm in Uusimaa.

2.3.3 Head circumference

Swedish boys have head circumference of 35.0 cm and girls 34.5 cm at birth when infants with birth weight less than 2500 grams and infants born outside Sweden were excluded (Werner & Bodin 2006). In India mean head circumference at 38 weeks was 33.9 cm for boys and 33.3 cm for girls (Kandraju et al. 2012).

Head circumference was on average 34.9 cm in Finnish infants in 2009-2010 (Vuori and Gissler 2011). Boys had larger head circumference (35.2 cm) than girls (34.6 cm).

2.4 Trends in size at birth

Size of birth in different populations changes continually over time and reflects the changes in environment, economical, societal and living conditions.

2.4.1 Prehistoric of size at birth

Based on archeological findings of adult skeletons researchers have estimated birth weights in different periods of time. In Palaeolithic period birth weight was estimated to have been about 3300 grams, then declining to 2700 to 2900 grams in Neolithic (Wells 2009). Since origin of the agriculture, birth weight was fairly staple, showing only minor increase, no change or modest decline in different populations until beginning of industrialization when birth weight started increase sharply.

2.4.2 From 18th century to the Second World War

Systematic measurements of infants started much more recently, there are some records of birth weight measurements from 18th century, but collecting of anthropometric data on newborns began in bigger extent just after the Second World War (Steckel 1998). Among women involved in domestic or unskilled labour in Edinburgh between 1847 to 1920 birth weight of their infants was on average about 3300 grams, but there was considerable fluctuation in birth weight decreasing about 400 grams in late nineteenth century and increasing slightly again in the beginning of twentieth century. In Vienna between 1865 to 1930 birth weight of infants was around 3100 grams, being quite stable until the First World War, decreasing during the war and increasing to almost 3300 grams in 1920’s. The proportion of low birth weight infants increased in both cities over the monitoring period.

2.4.3 1950’s to beginning of 2000’s in developed world

According to study made in the United States from 1950’s to 1990’s birth weight increased within families 33 grams in black male infants and 74 grams in white female infants (Chike-

Obi 1996). The proportion of very low birth weight infants increased 56 percent in black population, but in white population decreased by 6 percent. In another study examining low birth weight prevalence in whole population in United States it was found, that low birth weight prevalence increased from 1950's to late 1960's, decreased until 1980's and started to increase again steadily (Brosco et al. 2010). In Japanese infants birth weight, birth length and head circumference increased from the 1960's to 1970's, but between 1970's and 1980's birth weight and birth length remained stable and head circumference decreased (Oishi et al. 2004). In Finland head circumference increased from 1950's to end of 20th century and beginning of 2000's (Karvonen et al. 2012). Similar trend was seen with birth weight and length; mean birth weight and length was in 1950's to 1970's 3413 grams and 49.8 cm for boys and 3284 grams and 48.9 cm for girls and has increased to 3540 grams and 50.4 cm for boys and 3427 grams and 49.6 cm for girls in 2010 (Pihkala et al. 1989, Vuori and Gissler 2011).

2.4.4 Trends in developing world

From developing world trend data on birth weight is not available from over long time of period. In Iran the birth weight has decreased from 3222 grams to 3152 grams from 1970's to 2000's, but there has been no significant change in birth length (Mirmiran et al. 2013). In Vietnam there was a significant increase of birth weight and length from 1980's to 2000's (Hop le 2003). According to longitudinal DHS data on birth weight from 20 countries, prevalence of LBW has remained quite constant from 1990's to 2000 (24 percent and 23 percent) (UNICEF & WHO, 2004). Situation in South Asia and sub-Saharan Africa has shown no improvement or situation has even worsened (Measure DHS 2013).

2.4.5 Recent trends

In developed world increase of size at birth seems to have turned to opposite direction in past few decades. In Finland the average birth weight has decreased from 3548 grams in 1987 to 3483 grams in 2010 and birth length from 50.2 cm to 50.0 cm (Vuori and Gissler 2011). The prevalence of low birth weight has increased in most European countries, especially in

Greece, Malta, Portugal and Spain (OECD, 2013). However, in Poland and Hungary there has been opposite trend and in Nordic countries prevalence has remained stable.

Although the average birth weight and length have decreased in past few decades in many countries, in some countries proportion of macrosomic and LGA infants has increased. In China the prevalence of macrosomia rose from 6 percent in 1994 to 7.8 percent in 2005 (Lu et al. 2011). Also incidence of LGA increased, from 14 percent to 18 percentin the same period. Similar trend was seen in New South Wales, where LGA babies increased by 18 percent for boys and 21 percent for girls, with the average birth weight increasing simultaneously by 23 grams and 25 grams, respectively (Hadfield et al. 2009). Even bigger increase of LGA by 23 percent was seen in Sweden from 1992 to 2001 (Surkan et al. 2004).

2.5 Factors affecting size at birth

Many different factors affect infant size at birth. These factors can be related to the infant, mother or the environment where mother and fetus live. Understanding which factors affect size at birth is important, since it may provide us possibilities to impact these factors and thus improve size at birth to optimal. Factors affecting growth in fetal period may be genetic or environmental, but distinguishing these two is very difficult. It seems that genetics has the largest effect on size at birth, but also environmental modifiable factors correlate significantly with newborn size (De Stavola et al. 2011).

2.5.1 Genetics

Both fetal and maternal genes may affect size at birth. There is a complex interaction between parental and fetal genetic and environmental factors. Genes passed from both mother and father to the fetus influence fetal growth and size at birth (Yaghootkar & Freathy 2012). Maternal genes have also indirect effect to size at birth through intrauterine environment and external environment acts via intrauterine environment and genes to size of birth. Maternal genes contribute to infants’ size at birth through intrauterine environment even though child is biological to the mother (Rice & Thapar 2010). Fathers have also been shown to influence size at birth of their children (Klebanoff et al. 1998, Knight et al. 2005), but the effect is fairly small and maternal characteristics and intrauterine environment may inhibit largely this association (Rice & Thapar 2010).

Heritability of size at birth has been studied mostly with twin studies by comparing resemblance of monozygotic and dizygotic twin pairs. According to twin studies heritability of birth weight varies between 29 to 40 percent (Clausson, Lichtenstein & Cnattingius 2000, Moon-Kanamori et al. 2012). In other twin study genetic factors explained totally 70 percent of variation in birth weight, of which major part (over 50 percent) was caused by fetal genes and the rest (under 20 percent) by maternal genes (Magnus 1984).

Also intergenerational studies have been used in estimating heritability of fetal growth and size of birth. Lunde et al. (2012) estimated that both fetal and maternal genes explain 53 percent of the variation in birth weight, 50 percent in birth length and 46 percent in head circumference, the effect of fetal genetic factors being larger than maternal genetic factors (Lunde et al. 2012). In another intergenerational study, heritability estimate for birth weight was 26 percent in singletons (Mook-Kanamori et al. 2012).

Genetic factors may also affect gestational age, which in turn impacts size at birth (Lunde et al. 2012). Maternal genetic factors were more important in explaining gestational age (14 percent of the variation) than fetal genetic factors (11 percent of the variation). The effect of genetic factors on size at birth is not stable throughout pregnancy. Mook-Kanamori et al. (2012) estimated heritability for fetal weight to increase from 17 percent to 27 percent during second to third trimester. In contrast, Gielen et al. (2008) found heritability to decrease during gestation from over half (52 percent) at 25 gestational weeks to 30 percent at 42 gestational weeks in first born twins with separate placentas. If a mother has been SGA herself, she has 2.5 times greater risk of giving birth to a SGA child or 10 times greater risk if mother has earlier given birth to a SGA child (Dunkel 2010).

2.5.2 Environmental factors

2.5.2.1 Anthropometry of mothers

Maternal weight and height are associated to infant's size at birth. Often measured maternal anthropometric indices include pre-pregnancy weight, height and weight gain during pregnancy. Correlation between maternal shoe size and infant's birth weight has also been analysed, but no such association was found (Stephens et al. 2006).

If mother's weight is high before pregnancy, it is more likely that her child is heavier than those of normal or underweight mothers. Every 1 kg increase in pre-pregnancy weight was associated with increase in birth weight of 260 g (Nahar, Mascie-Taylor & Begum 2007). Also maternal BMI has linear positive association with birth weight (Friedlander et al. 2009, Stamnes Koepp et al. 2012). Maternal weight has been associated also with fetal size; in study by Thame, Osmond & Trotman (2012), larger maternal weight was associated with increased abdominal circumference and femoral length at 25 weeks and larger abdominal and head circumference and longer femur ten weeks later. Mother's own or grandparents' birth weights may be also associated with infant's size at birth. Maternal birth weight had strong effect on fetal growth and size at birth (Klebanoff & Yip 1987) and in other study it was concluded that every 100 gram increase in maternal birth weight was associated with 25 gram increase in birth weight (Stein and Lumey 2000). When comparing grandparent's and grandchildren's size at birth, results showed stronger correlation between grandchildren and maternal grandparents than paternal grandparents (De Stavola, Leon & Koupil 2011). However shared environmental factors, such as sociodemographic and behavioral factors, contributed to these associations.

Maternal height has also been associated with size at birth, both weight and length. Witter and Luke found infants of taller women to be significantly taller and heavier than children of shorter women, but the association was seen only from 35 weeks onward (Witter & Luke 1991). However, in a more recent study it was found that maternal height is associated with femoral length and head circumference already at 25 weeks (Thame, Osmond & Trotman 2012). There might be ethnic differences in association between maternal height and size at birth, in Hispanic mother-child pairs no such association were found (Pickett, Abrams &

Selvin 2000). Maternal short height also increases risk of low birth weight (Elshibly & Schmalisch 2008).

Maternal weight gain during pregnancy consists of fetus (3-4kg), amniotic fluid (0.5-1kg), placenta (0.5-0.6kg), increase in blood volume (1.2kg) and fat accumulating to mother's body (Rasmussen and Yaktine 2009). Also edema is common in prenatal period and might affect weight gain. Most of the weight gain occurs in third trimester. Actual prenatal or target weight gain is individual and depends on maternal BMI before pregnancy. For underweight mother recommended weight gain is 12.5 – 18 kg, for normal weight mother 11.5 – 16 kg, for overweight 7 – 11.5 kg and for obese mother 5– 9 kg. Weight gain deviating from recommendations has been associated to adverse birth outcomes, such as Caesarean section, birth weight < 2500 grams or > 4000 grams, LGA, SGA, gestational hypertension or augmentation of labor (Crane et al. 2009, Rode et al. 2007, Park et al. 2011). Low maternal weight gain has been associated with the risk of SGA (Bamfo & Obido 2011). There is conflicting results about weight gain rate in different periods of pregnancy; a study suggests weight gain in second trimester would influence the most birth weight (Sekiya et al. 2007), in the other study first trimester weight gain predicted newborn size more strongly than the weight gain in second or third trimester (Brown et al. 2002) and also there are studies highlighting the importance of third trimester for infants size at birth (Abrams & Selvin 1995, Strauss & Dietz 1999).

2.5.2.2 Placenta

Placenta is connecting organ between fetus and uterine wall, allowing transport of nutrients and oxygen from mother to fetus and waste products from fetus to mother. Placenta has essential role ensuring optimal fetus development and growth and disturbances in placental functional capacity may result overgrowth or growth restriction of fetus (Roland et al. 2012). Increasing size of the placenta increases its functional capacity; nutrient and oxygen transport to fetus and has been linked with increased size at birth. One gram increase in placenta weight increases birth weight almost two grams, but the relation was nonlinear (Sanin et al. 2001). In normal infant, size of placenta is expected to be certain for the certain birth weight. Thus proportion of placental weight to birth weight could be used as an indicator for growth restriction of fetus (Hemachandra et al. 2006). High or low ratio of placental weight to birth weight has been found to correlate also with other adverse perinatal outcomes, such as admission to intensive care, Apgar scores and Caesarean section or death (Haavaldsen, Samuelsen & Eskild 2013, Shehata et al. 2011). Ratio of placental weight for birth weight could be used as an indicator for nutritional status when information of birth length or head circumference is not available (Williams, Gore & O'Brien 2000). In addition to size of placenta, also placental thickness and area affect placental function. Large placental area and increased thickness have been associated with larger birth weight (Salafia et al. 2007).

2.5.2.3 Parity

Parity, the number of times mother has given birth, is a significant determinant for size at birth. In general first children are smaller than subsequent children and this is suspected to be due to changes in maternal metabolism or changes in uterus blood flow in subsequent pregnancies (Camilleri & Cremona 1970, Hafner et al. 2000). First children are about 200 grams lighter than second children and first born children are at greater risk of LBW and SGA (Ong et al. 2002, Shah 2010). Similar tendency can be seen also in Finnish children, but to a smaller extent (Vuori & Gissler 2011). In addition, although lighter at birth, being born first is associated with faster growth, elevated adiposity and increased risk for metabolic disorders later in life (Siervo et al. 2010). There is a greatest increase in birth weight between first and second children and similar, but smaller tendency exists also with subsequent children (Swamy et al. 2012). Most of the studies evaluating association between size at birth and parity have mainly focused on birth weight. Only one study was found about other measures taken at birth; birth length and head circumference, and parity, but they found only association between birth weight and parity (Feleke & Enquosalassie 1999).

2.5.2.4 Smoking

In Finland, about 15 percent of pregnant women smoke during pregnancy (Tiitinen 2012). Tobacco contains thousands of hazardous chemicals, of which many penetrate through placenta to the fetus increasing infant growth-restriction, morbidity and mortality. The exact mechanism behind the effects of smoking to fetus has not been proven, but it is suggested to consist of multiple different factors. For example nicotine and carbon monoxide in tobacco deteriorates uterus and placental blood flow causing decreased oxygen uptake by fetus. Fetus exposure to tobacco impairs fetal growth and may also shorten gestational length, causing preterm births (Abel 1980, Rogers 2008, Tiitinen 2012). Smoking reduces both birth weight and length although birth weight is more strongly associated than birth length with maternal smoking (Schell & Hodges 1985). Estimates, on how large is the decrement of birth weight varies between 150 to 377 grams, depending on the number of cigarettes smoked per day (Meyer & Comstock 1972, Wang, Zuckerman & Pearson 2002). Mothers are advised to quit smoking already before pregnancy, which is the best solution, but also reduction or quitting at later stage of pregnancy has been shown to be beneficial for the pregnancy outcome (Bernstein et al. 2005). Although mothers don’t smoke, fetus might be exposed to passive smoking, which also affects size at birth, although in smaller extent than maternal smoking. A systematic review and meta-analysis found that passive smoking reduces birth weight more than 33 grams, increases risk of LBW, but has no effect on gestational age or risk of SGA (Leonardi-Bee et al. 2008). In a study made in Saudi Arabia, passive smoking was associated with both 35 g lower birth weight and 0.26 cm shorter birth length (Wahabi et al. 2013). Smoking might affect birth weight even by tobacco use of previous generations during maternal prenatal period (Misra, Astone & Lynch 2005).

2.5.2.5 Socioeconomic factors

Socioeconomic factors, such as family income, parental education, occupation and access to health care and other resources are associated with human health and wellbeing and affect also birth outcome. These social determinants may be individual or area based, but the outcome to infant’s size is similar (Weightman et al. 2012). Average size of birth is smaller and LWB and SGA more prevalent in developing countries compared with economically better off countries (Black et al. 2008, de Onis, Blössner & Villar 1998). Also inside countries socioeconomically more advantageous areas show lower prevalence of LBW than in disadvantage areas (Spencer et al. 1999) and the risk for SGA is greater in mothers with low socioeconomic status (Bamfo and Obido 2011). When studying the trends of size at birth in Russia, U-shaped curve was seen in birth weight and length, values being lowest in 1990’s when economic transition was starting (Mironov 2007). No single sole reason has been found behind the adverse effects of socioeconomic factors, although multiple issues such as high prevalence of teenage pregnancies, maternal stress or lack of health care services in the area have been suggested to cause decreased size at birth (Weightman et al. 2012).

2.5.2.6 Altitude

Altitude of habitat has been shown to affect size at birth. Living in high altitude is associated with smaller birth weight, length and may also affect gestational length (Haas et al. 1982, Hartinger et al 2006, Wenhby, Castilla & Lopez-Camelo 2010). Mechanism for this effect is suggested to be mediated by low oxygen level available for the fetus due to lower air pressure at high altitudes. The negative effect may not be seen in all ethnic groups, in Papua New Guinea altitude did not have growth-retarding effect (Primhak & MacGregor 1991), or the effect may be smaller in populations' resided long time in high altitudes compared to more recently migrated populations (Moore 2000). Why some populations are more prone to negative effects of altitude is not known thoroughly, but this is suggested to be due to genetic factors or population specific metabolic features which have developed over long period of time (Julian et al. 2011). It may take more than three generations living in high altitudes before protecting effect could be detected. The effect of altitude depends also on the gestational age at birth; according to Hartinger et al. (2006), altitude has greatest effect on infants born after 36 weeks.

2.6 Consequences of abnormal size at birth

Both too large and too small size at birth has been associated with ill health and risk of death in many studies.

2.6.1 Small size at birth

It has been estimated, that low birth weight increases infants' risk of dying during the first year 20-fold compared to normal weight babies (UNICEF & WHO, 2004(Pulver et al., 2009)). Low birth weight contributes also to other health outcomes and is an important indicator of both infant and mothers wellbeing. Infant's survival was 96 percent in infants weighing 1251 to 1500 grams and 55 percent in infants weighing 501-750 grams in the first 120 days of life in the United States (Fanaroff et al. 2007). Sex had an impact on the risk of death; mortality was more prevalent among low birth weight boys than girls. A Finnish study has also shown small size at birth to be a predictor of increased mortality in adulthood (Kajantie, Osmond & Barker 2005). Low birth weight and short length were associated with increased all-cause mortality among women and cardiovascular mortality among men.

SGA is also associated with increased morbidity and mortality. SGA infants are at greater risk for subnormal growth and smaller size for all weight, height and head circumference, neurodevelopmental delays or dysfuctions, cardiovascular disease, type 2 diabetes and renal disease (Hack et al. 2003, Hediger et al. 1998, Noeker 2003, Saenger et al. 2007). However risk of mortality and morbidity depend much on the etiology of SGA; children with IUGR have a bigger risk for complications than innately SGAs (Bamfo and Obido 2011, Marconi et al. 2008).

Low weight to length; low PI with SGA has been associated with asphyxia, acidosis, hypoglycemia, hypothermia and hyperviscosity (Walther & Ramaekers 1982). Low weight to length ratio has also been correlated with increased mortality, even in children who are not SGA (Williams & O'Brien 1997). Small head circumference has been associated with poorer cognitive ability and lower IQ later in childhood (Broekman et al. 2009, Veena et al. 2010).

2.6.2 Large size at birth

Large size at birth has been associated with maternal and fetal complications both in short and long term. Neonatal complications include shoulder dystocia and associated brachial plexus injury, perinatal asphyxia, meconium aspiration, hypoglycaemia and death (Boulet et al., 2003; Henriksen 2008; Linder et al.; 2014; Raio et al., 2003; Rossi et al., 2013). In a study by Baker, Olsen and Sorensen (2008) infants with high birth weight (4251-5500 g) had 7 percent higher all-cause mortality than normal birth weight infants. In a long term, high birth weight has been associated with increased risk of developing obesity, diabetes, cancer and cardiovascular disease (Baird et al., 2005; Hediger et al., 1998; Ross, 2006). Also higher risks for caesarean delivery and maternal complications, such as chorioamniotis, fourth-degree perineal lacerations, postpartum hemorrhage and prolonged hospital stay have been associated with large birth weight (Stotland et al., 2004). Macrosomia can be divided to two different types; proportionate and disproportionate macrosomia, the latter refers to a high weight/ length ratio and is suggested to be associated with increased risk of complications compared to proportionate macrosomia (Djelmis et al. 1998). Thus birth weight is not the only determinant of macrosomia related complications and also information on body proportions, composition and metabolic characteristics should be taken into consideration in risk estimations.

LGA infants grow to be later in life taller, heavier and have larger head circumference than SGA infants (Hediger et al. 1998). LGA is associated with both maternal and neonatal complications. Maternal complications include increased risk of cesarean section, perineal lacerations, postpartum hemorrhage and prolonged hospital stay (Stoland et al. 2004, Weissmann-Brenner et al. 2012). Shoulder dystocia, neonatal hypoglycemia and longer hospitalization are common neonatal complications. Health risks for both mother and child increases with increasing weight. LGA may also be associated with long term health risks such as diabetes, hypertension, asthma or cancer (Baker, Olsen & Sorensen 2008, Kajantie et al. 2005, Ng et al. 2010).

High ratio of weight to length at birth and high PI has been associated with the risk of being overweight in adulthood (Pietiläinen et al., 2001; Tuvemo, Cnattingius & Jonsson, 1999). Risk of cancer death is higher in males with high birth weight or high PI, but not in females (Kajantie et al., 2005).

2.7 Causality; morbidity, mortality and size at birth

There is sound evidence of birth weight being a strong predictor of adverse health consequences or death, but the debate remains about causality of size of birth to increased mortality or morbidity (Wilcox 2001). The categories used to classify size at birth are also criticized for being uninformative and inappropriate for the current use as an indicator and target of infant survival and health.

In populations having high prevalence of low birth weight, also the risk of death among infants is higher (UNICEF & WHO, 2004). However in populations where both low birth weight and infant mortality are common, proportionally less low birth weight babies die than in better-off populations (Wilcox 2001, Wilcox et al. 1995). This is called a paradox of low birth weight and it holds true in many groups of infants having high mortality rates, such as infants born to smoking mothers (Hernàndez-Díaz, Schisterman & Hernàn 2006). According to the Wilcox-Russel hypothesis size at birth is associated with health and risk of death, but is not the causal path to morbidity or mortality (Wilcox 2001). There may be some other confounding factors affecting both size and mortality or morbidity, and size of birth can change without affecting mortality or morbidity. The hypothesis is based on the normal distribution of size at birth with specific mortality or morbidity curve shifting simultaneously. This can be in response of some covariate or covariate may have direct effect on mortality at all birth weights. Hypothesis has been proven for maternal age (Gage et al. 2009).

This kind of hypothesis is important to consider when exploring for the best indicators for infant health and survival. Even if size of birth would not be a causal link to morbidity and mortality, using it as an indicator is favored by the facts that it is easy to measure, widely used in different populations and correlates with many adverse health outcomes. However, infant size measures, birth weight, length and head circumference should not be used as endpoints in public health efforts to improve health and decrease risk of death.

3 AIMS

Using categorization based only on birth weight leaves unacknowledged other infant size measures, which may be important for infant and maternal morbidity. The objective is to study whether anthropometric measures; birth length and head circumference in addition to birth weight taken during childbirth are associated to health risks and conditions related in literature to macrosomia or LGA using data from Birth Register from 1 January 2008 to 31 March 2010 from Southwestern Finland. The specific aims are:

1. To estimate the prevalence of macrosomia (>4000g) and LGA and adverse maternal and infant health conditions related to large birth weight.
2. To determine the effects of newborn body size measured with birth length and head circumference on these health conditions.

4 SUBJECTS AND METHODS

4.1 Study population

Data on all births and newborns are gathered in the Medical Birth Register by the Finnish National Institute for Health and Welfare (THL). Register contains data on all live births and on stillbirths of fetuses with a birth weight of at least 500 g or with a gestational age of at least 22+0 weeks. Register contains data on characteristics of the mother, antenatal care, delivery and perinatal outcomes. Data on mother include age, weight and height, profession, marital status, chronic illnesses and parity and mother's health conditions during pregnancy and place and mode of delivery. Data on newborn include anthropometric measures; weight, length and head circumference, sex, plurality, gestational age based on the maternal report on last menstrual period and ultrasound assessment, hospitalization, morbidity and mortality. The register covers nearly all births and data has been found to correspond well or satisfactorily with the hospital records in several quality analyses (Gissler and Shelley, 2002; Gissler et al., 1995; Teperi, 1993). For this study, we used the Birth Register data from 1 January 2008 to 31 March 2010 from Southwestern Finland. Only singleton, live births and term (>37 gestational weeks) pregnancies were included to the analysis (n=10006) and fetal anomalies were excluded. Our study population consists of the STEPS study, which aims to search for the precursors and causes of problems in child health and well-being by using a multidisciplinary approach (Lagström et al., 2013). The STEPS study protocol was approved by the Ethics Committee of the Hospital District of South-West Finland in 2008 and permission to use the register data were obtained from the National Institute for Health and Welfare (THL). Informed consent of the individuals was not asked and individuals were not contacted since data was analyzed anonymously.

4.2 Variables and definitions

Variables used in this study can be found from Table 1. The weight, crown-heel length and head circumference observations were checked for possible outlier values and two outliers of length and three of head circumference were found and removed from the data. In addition two size measures; ponderal index (PI) and brain - body weight ratio (BBR) were calculated. Ponderal index (PI) was used as an indicator of newborn thinnes / fattness and brain - body weight ratio (BBR) as an indicator of head to body proportionality derived from the National Institute of Neurological and Communicative Disorders and Stroke's Collaborative Perinatal Project (McLennan JE, Gilles FH, Neff RK 1983). PI was calculated as [weight in g / (crown-heel length in cm)^3]*100 and BBR 100 x (0,037 x head circumference in cm^{2,57})/birth weight in g. The higher the PI is, the fatter and shorter newborn is and the lower the PI, the thinner and longer newborn is. As for BBR, a higher value means larger proportion of the weight residing in the brain and lower value lower proportion of weight residing in the brain. Outcome variables were chosen based on previous studies. Birth outcomes for both newborn and mother included: perinatal asphyxia, shoulder dystocia, hypoglycemia, Apgar scores 1 min and 5 min, treatment and monitoring at IUC, unplanned cesarean section, prolonged labor 1st and 2nd stage, hospital stay of the mother, postpartum hemorrhage, perineal trauma, any medical pain relief during delivery. Also mortality, brachial plexus injury, meconium aspiration, transient tachypnea, hyperthermia, hypocalcemia and polycythemia has been associated with high birth weight, but were not included in the analysis because of exiguity or non-existence of the cases. The Medical Birth Register data contains diagnoses with ICD-10 codes and also check-box questions and both of these were used depending on the variable. Data on perinatal asphyxia, cesarean section, Apgar scores, treatment at or monitoring at the ICU, hospital stay of the mother and the use of medical pain relief were received from check-box questions.

Macrosomia was defined as birth weight over and 4000g. The new Finnish population-based references were used to determine sex- and gestational age standard deviation scores (SDs) for birth weight, length and head circumference (Sankilampi et al., 2013). Macrosomic newborns were grouped into three almost equal classes of birth length and head circumference. PI and BBR were used as continuous variables. Outcome variables; asphyxia, treatment at or monitoring at the ICU and the use any medical pain relief during delivery were used as dichotomous variables, yes and no. Those who had had unplanned cesarean section were compared with cases of normal vaginal deliveries, Apgar scores 1 and 5 minutes were classified as low (< 6) or normal (>6), and hospital stay divided into above or below the mean (3 days in TYKS, Vuori and Gissler, 2011). Dichotomous variables, no and yes, were also formed with ICD-10 codes (Table 1) from shoulder dystocia, hypoglycemia, infection of amniotic sac and membranes, prolonged labour 1st stage, prolonged labour 2nd stage, postpartum hemorrhage and third degree and fourth degree perineal trauma.

Table 1. Variables included in this study

Predictor variables	Definition
Macrosomia	Birth weight (BW) > 4000g
Standard deviation scores (SDs)	Calculated for birth weight (BW), birth length (BL) and head circumference (HC) [a]
Ponderal index (PI)	Measure of thinnes / fatness Birth weight in grams/(length in cm)^{3}x100
Brain - body weight ratio (BBR)	Measure of head to body proportionality 100 x (0,037 x head circumference in cm^{2,57})/birth weight in g

Outcome variables	Definition
Prolonged labor 1st stage	ICD-code O63.0
Prolonged labour 2nd stage	ICD-code O63.1
Caesarean section, unplanned	Caesarean section, not including elective CS
Hospital stay mother	Mean hospital stay 3 days in TYKS 2010[b] < 3days and ≥ 3days
Postpartum hemorrhage	Composite outcome from ICD-code O72.1 and ICD-code O72.2
Perineal trauma, 3 or 4- degree	Composite outcome from ICD-code O70.2 and ICD-code O70.3
Medical pain relief	The use of any medical pain relief as composite outcome Yes / no
Perinatal asphyxia	Yes / no
Shoulder dystocia	Obstructed labour due to shoulder dystocia (Impacted shoulders), ICD-code O66.0

Hypoglycemia	Plasma glucose < 2.6mmol/l, P70.4
Chorioamnionitis	Infection of amniotic sac and membranes (Amnionitis, Chorioamnionitis, Membranitis and Placentitis), O41.1
Apgar score 1min	Normal > 6, low ≤ 6
Apgar score 5min	Normal > 6, low ≤ 6
Treatment or monitoring at the hospital	Treatment or monitoring at ICU or other hospital ward

[a] Sankilampi et al. 2013

[b] Vuori and Gissler, 2011

4.3 Statistical analysis

Statistical differences in the prevalence of maternal and infant health outcomes of newborns with BW of 1) ≤ and > 4000g, 2) ≤ 4000g, > 4000g to 4500g and < 4500g and 3) AGA and LGA newborns were evaluated by χ^2 test and Fisher's exact test. The test the association between crown heel birth length and head circumference in macrosomic newborns and birth outcomes was also studied with χ^2 test and Fisher's exact test. Logistic regression analyses were used to assess probability of each significant birth outcome with newborn BL and HC in macrosomic newborn (BW > 4000g), reporting odds ratios and 95 percent confidence intervals. Three classes of BL or HC were used in logistic analysis as dummy variables, smallest BL / HC class as reference category. In addition PI and BBR were used in logistic analysis as continuous predictor variables. The data were analyzed with SPSS statistical software package (version 21.0; SPSS Inc., Chicago, IL, USA). Statistical level of significance was set to 0.05 in all analyses.

5 RESULTS

The study population included 10006 term singleton births, of which three newborns died during or after birth. Mean maternal age at birth was 30.2 years (SD 5.1) and 44.1% of the mothers were primiparous. Most of the mothers were either married or cohabiting (94.2%) and had Finnish citizenship (93.1%). Mothers mean weight before pregnancy was 67.4kg (SD 14.1) and height 166.1 cm (SD 6.1). Gestational age at birth varied from 37+0 to 43+4 weeks and only 13 babies were born outside elsewhere than in hospital or in the way to hospital. Majority of babies were born by spontaneous vaginal delivery (78.6%), 9% with assisted vaginal delivery (vacuum, breech or forceps) and 12.2% with cesarean section, either planned or unplanned.

Mean birth weight was 3582g (SD 466), birth length 50.9cm (SD 2.0) and head circumference 35.1cm (SD 1.4) and 50.6% of the babies were boys and 49.4% girls. Eighteen percent of the newborns had birth weight over 4000g and were thus defined as macrosomic, 2.6% had BW above 4500g and 2.2% were classed as LGA by weight, 4.2% had birth length and 2.8% head circumference over 2SDs. The mean PI was 2.7cm/g^3, with the range extending from 1.74 to 4.12 cm/g^3. The mean BBR was 9.8, with the range from 6.9 to 15.1.

5.1 Relation between birth weight and health outcomes

The results from the analysis of the association between macrosomia and complications of birth, maternal and newborn outcomes are presented in Table 2. There were more cases of prolonged labor at first and second stage with macrosomic newborns than newborns with normal weight. Also unplanned cesarean section was the mode of birth more often for macrosomic than normal weight newborns. Postpartum hemorrhage, third or fourth degree perineal trauma and the use of medical pain relief during birth were more common among macrosomic than normal weight newborns. However, hospital stay of the mothers who had macrosomic newborn was shorter than for mothers having normal weight newborn. Of neonatal complications, shoulder dystocia, hypoglycemia, low Apgar score at 1 min and treatment or monitoring at ICU were more common among macrosomic, than normal weight newborns, but perinatal asphyxia was found to be more common among normal weight than macrosomic newborns. We did not find hypoglycemia, chorioamnionitis or Apgar score at 5min to be associated with macrosomia.

Table 2. Number and prevalence of birth outcome indicators in macrosomic or normal weight newborns analysed with χ^2 test and Fisher's exact test.

	Normal BW ≤ 4000g (n=8237)		Macrosomic BW > 4000g (n=1796)		
Complications of birth	n	%	n	%	*p*
Prolonged labor 1st stage	93	1,1	66	3,7	< 0,001
Prolonged labor 2nd stage	239	2,9	72	4,1	0,01
Caesarean section, unplanned	540	7,7	150	9,8	0,007
Maternal birth outcomes					
Hospital stay, ≥ 3 days	4392	54,8	843	49,0	< 0,001
Postpartum hemorrhage	476	5,8	172	9,7	< 0,001
Perineal trauma, 3rd or 4th degree	80	1,0	29	1,6	0,014
Using medical pain relief	6468	78,5	1458	79,4	< 0,001
Neonatal birth outcomes					
Perinatal asphyxia	589	7,4	103	5,8	0,046
Shoulder dystocia	6	0,1	8	0,4	< 0,001
Hypoglycemia	72	0,9	19	1,1	0,422
Chorioamnionitis	12	0,1	3	0,2	0,738
Low Apgar score 1min (≤ 6)	472	5,7	146	8,3	< 0,001
Low Apgar score 5min (≤ 6)	125	1,5	28	1,6	0,839
Treatment or monitoring at hospital	559	6,8	159	9,0	0,001

We also divided macrosomic newborn into two categories to study, whether increasing weight increased adverse outcomes at birth (Table 3). Incidence of prolonged labor at first stage, unplanned caesarean section, maternal postpartum hemorrhage, neonatal shoulder dystocia and treatment and monitoring at the hospital ward was greater in the newborn having birth weight larger than 4500g than in normal weight newborns. Also hypoglycemia, for which we did not observe association with birth weight above 4000g, was occurring significantly more often with newborn with birth weight above 4500g, than in newborn with normal weight or weight between 4000 to 4500g. Prolonged labor at second stage of labor, maternal perineal trauma, the use of medical pain relief during labor and low Apgar score were most prevalent in newborn having birth weight between 4000 to 4500g. Groups did not differ significantly in prevalence of neonatal asphyxia, chorioamnionitis or Apgar score at 5min.

Table 3. Number and prevalence of birth outcome indicators in normal weight newborns and macrosomic newborns with birth weight of 4001 to 4500g or over 4500g, analysed with χ^2 test and Fisher's exact test.

	Normal		Macrosomic				
	BW ≤ 4000g (n=8237)		BW = 4001-4500g (n=1508)		BW > 4500g (n=261)		
Complications of birth	n	%	n	%	n	%	*p*
Prolonged labor 1st stage	93	1,1	55	3,6	11	4,2	< 0,001
Prolonged labor 2nd stage	239	2,9	62	4,1	10	3,8	0,036
Caesarean section, unplanned	540	7,7	126	9,6	24	10,7	0,023
Maternal birth outcomes							
Hospital stay, ≥ 3 days	4392	54,8	712	48,6	131	51,4	< 0,001
Postpartum hemorrhage	476	5,8	132	8,8	40	15,3	< 0,001
Perineal trauma, 3rd or 4th degree	80	1,0	27	1,8	2	0,8	0,017
Using medical pain relief	6468	78,5	1254	83,2	204	78,2	< 0,001
Neonatal birth outcomes							
Perinatal asphyxia	589	7,2	91	6,0	12	4,6	0,095
Shoulder dystocia	9	0,1	10	0,7	5	1,9	< 0,001
Hypoglycemia	72	0,9	12	0,8	7	2,7	0,009
Chorioamnionitis	12	0,1	3	0,2	0	0	0,810
Low Apgar score 1min (≤ 6)	472	5,7	125	8,3	21	8,0	< 0,001
Low Apgar score 5min (≤ 6)	125	1,5	25	1,7	3	1,1	0,839
Treatment or monitoring at hospital	559	6,8	125	8,3	34	13,0	0,001

As macrosomia, also birth weight for gestational age, classified as appropriate for gestational age (AGA) and large for gestational age (LGA) was associated with many complications of birth, maternal outcomes and newborn outcomes. The results are presented in Table 4. All complications of birth; prolonged 1st stage of labor, 2nd stage of labor and unplanned cesarean section were more common among LGA newborns than AGA newborns. Of maternal outcomes only postpartum hemorrhage and of neonatal outcomes shoulder dystocia, hypoglycemia and treatment and monitoring at ICU were significantly associated with birth weight for gestational age. We did not find maternal perineal trauma, the use of medical pain relief, asphyxia, chorioamnionitis or Apgar scores at 1 or 5 min to be associated with birth weight for gestational age. Although not significant association was not found with perinatal asphyxia and birth weight categories, there were a tendency of smaller prevalence in highest weight group.

Table 4. Number and prevalence of birth outcome indicators in AGA and LGA newborns analysed with χ^2 test and Fisher's exact test.

	AGA (n=9528)		LGA (n=225)		
Complications of birth	n	%	n	%	*p*
Prolonged labor 1st stage	149	1,6	9	4,0	0,011
Prolonged labor 2nd stage	838	13,4	26	22,4	0,001
Caesarean section, unplanned	614	7,5	56	16,6	< 0,001
Maternal birth outcomes					
Hospital stay, ≥ 3 days	4945	53,3	144	67,0	< 0,001
Postpartum hemorrhage	601	6,4	35	15,6	< 0,001
Perineal trauma, 3rd or 4th degree	104	1,1	4	1,8	0,318
Using medical pain relief	6322	83,9	126	83,4	0,874
Neonatal birth outcomes					
Perinatal asphyxia	637	6,7	11	6,6	0.285
Shoulder dystocia	11	0,1	3	1,4	< 0,001
Hypoglycemia	66	0,7	8	3,6	<0,001
Chorioamnionitis	14	0,1	1	0,4	0,296
Low Apgar score 1min (≤ 6)	583	6,1	16	6,1	0,540

Low Apgar score 5min (≤ 6)	143	1,5	3	1,3	0,564
Treatment or monitoring at hospital	625	6,6	36	16,0	< 0,001

5.2 Relation between birth length and health outcomes

When using χ^2 and Fisher's exact test, macrosomic newborns were grouped into three equal sized groups by birth length; ≤ 51cm, 52-53cm and ≥54cm, to compare variation in adverse birth outcomes with each of these birth length classes (Table 5). Since in previous analysis birth weight as such, seemed to be best predictors of birth outcomes studied, only macrosomic newborn with BW above 4000g were chosen for these analysis. Newborn with BW above 4500g were not used in analysis as a separate category, since they did not differ greatly from newborn with birth weight from 4000g to 4500g and also number of newborn in this category would have been too small for analysis. Chorioamniotitis, Apgar score at 5 minute were left out from the outcome variables, since they were not significantly associated with birth weight in any of the previous analysis.

Table 5. Number and prevalence of birth outcome indicators in macrosomic newborns in three birth length (BL) classes analysed with χ^2 test and Fisher's exact test.

	BW > 4000g						
	BL≤ 51cm (n=270)		BL = 52-53cm (n=776)		BL≥54cm (n=693)		
Complications of birth	n	%	n	%	n	%	*p*
Prolonged labor, 1st stage	5	1,9	25	3,2	35	5,1	0,038
Prolonged labor, 2nd stage	6	2,2	22	2,8	41	5,9	0,003
Caesarean section,unplanned	18	7,3	54	7,9	77	13,1	0,003
Maternal birth outcomes							
Hospital stay, ≥ 3 days	131	50,6	334	44,0	360	53,3	0,002
Postpartum hemorrhage	28	10,4	62	8,0	80	11,5	0,068

Perineal trauma, 3rd or 4th degree	4	1,5	9	1,2	14	2,0	0,410
Using medical pain relief	197	73,0	657	84,7	581	83,8	<0,001
Neonatal birth outcomes							
Perinatal asphyxia	8	3,0	44	5,7	48	6,9	0,059
Shoulder dystocia	1	0,4	0,3	0,3	11	1,6	0,012
Hypoglycemia	2	0,7	4	0,5	13	1,9	0,036
Low Apgar score 1min (≤ 6)	14	5,2	51	6,6	66	9,5	0,029
Treatment or monitoring at hospital	22	8,1	50	6,4	71	10,2	0,030

Birth length was associated significantly with all complications of birth, maternal hospital stay duration, the use of medical pain relief during labor, neonatal birth outcomes; shoulder dystocia, hypoglycemia, Apgar score at 1 minute and treatment and monitoring at the hospital. Macrosomic newborn with large birth length had highest prevalence of all outcome variables, except the use of medical pain relief during labor.

Association between birth length and birth outcomes was further studied with logistic regression analysis using BL categories as dummy variables and the lowest length category as reference length (Table 6). Higher birth length as compared to the shortest category in macrosomic newborn was associated with an increasing relative risk for prolonged labor at first stage, maternal postpartum hemorrhage and the use of medical pain relief during labor, expressed as odds ratio (OR). For prolonged labor at second stage, unplanned caesarean section, maternal perineal trauma, neonatal shoulder dystocia and hypoglycemia, low Apgar score at 1 minutes and treatment or monitoring at the hospital, risk was significantly higher only in longest infants, having birth length over or equal to 54 cm. Whereas risk for longer than average hospital stay of mother was smaller for average size newborn, compared to short newborn in the reference category.

Table 6. Odds ratios, confidence intervals and p-values for outcome variables by three birth length (BL) categories in macrosomic (>4000g) newborns. Smallest BL category is used as reference length.

Outcome variable	Birth length category	OR	CI 95%	*p*
Prolonged labor 1st stage	≤ 51cm	1,0		
	= 52-53cm	2,837	1,818 - 4,428	<0,001
	≥ 54cm	4,534	3,059 - 6,720	<0,001
Prolonged labor 2nd stage	≤ 51cm	1,0		
	= 52-53cm	0,975	0,627 – 1,518	0,911
	≥ 54cm	2,102	1,496 – 2,953	<0,001
Caesarean section, unplanned	≤ 51cm	1,0		
	= 52-53cm	1,029	0,769 – 1,377	0,846
	≥ 54cm	1,809	1,402 – 2,333	<0,001
Maternal hospital stay	≤ 51cm	1,0		
	= 52-53cm	0,652	0,561 – 0,757	<0,001
	≥ 54cm	0,948	0,810 – 1,109	0,502
Postpartum hemorrhage	≤ 51cm	1,0		
	= 52-53cm	1,378	1,047 – 1,814	0,022
	≥ 54cm	2,071	1,614 – 2,659	< 0,001
Perineal trauma, 3th or 4th degree	≤ 51cm	1,0		
	= 52-53cm	1,153	0,578 – 2,300	0,686
	≥ 54cm	2,026	1,146 – 3,584	0,015
Medical pain relief	≤ 51cm	1,0		
	= 52-53cm	1,526	1,247 – 1,868	< 0,001
	≥ 54cm	1,434	1,164 – 1,767	0,001
Perinatal asphyxia	≤ 51cm	1,0		
	= 52-53cm	0,795	0,580 – 1,090	0,154
	≥ 54cm	0,919	0,726 – 1,335	0,919
Shoulder dystocia	≤ 51cm	1,0		
	= 52-53cm	2,003	0,443 – 9,053	0,367
	≥ 54cm	12,501	5,400 – 28,940	< 0,001
Hypoglycemia	≤ 51cm	1,0		
	= 52-53cm	0,593	0,216 – 1,625	0,309
	≥ 54cm	2,186	1,206 – 3,962	0,010
Low Apgar score	≤ 51cm	1,0		

1min (≤ 6)	= 52-53cm	1,128	0,838 – 1,520	0,427
	≥ 54cm	1,688	1,290 – 2,210	< 0,001
Treatment or monitoring ICU	≤ 51cm	1,0		
	= 52-53cm	0,916	0,680 – 1,234	0,564
	≥ 54cm	1,518	1,171 – 1,967	0,002

To further study the association between birth length or body proportionality by weight and length and birth outcomes with logistic regression, new composite variable ponderal index (PI) was combined from weight and length. Since birth weight and length correlated strongly with each other (R=0,752, p<0,001), weight and length could not be used as individual predictor variables. The results are presented in Table 7.

Table 7. Logistic regression analyses of prevalence of outcome variables in relation to ponderal index (PI). Odds ratios (OR), confidence intervals (CI 95%) and p-values.

	OR	CI 95%	p
Prolonged labor 1st stage	0,542	0,280-1,048	0,068
Prolonged labour 2nd stage	0,434	0,268-0,704	0,001
Caesarean section, unplanned	0,320	0,228-0,450	<0,001
Hospital stay mother	0,505	0,427-0,596	<0,001
Postpartum hemorrhage	1,299	0,938-1,798	0,115
Perineal trauma, 3 or 4- degree	0,403	0,178-0,913	0,030
Medical pain relief	0,497	0,408-0,605	<0,001
Perinatal asphyxia	0,123	0,087-0,175	<0,001
Shoulder dystocia	8,293	1,552-44,30	0,013
Hypoglycemia	0,481	0,201-1,154	0,101
Chorioamniotitis	0,892	0,105-7,603	0,917
Low Apgar score 1min (≤6)	0,285	0,196-0,415	<0,001
Low Apgar score 5min (≤6)	0,104	0,043-0,254	<0,001
Treatment or monitoring at hospital	0,448	0,316-0,635	<0,001

PI was statistically significantly associated with prolonged labor in the 2nd stage, caesarean section, hospital stay of the mother, perineal trauma, the use of medical pain relief, perinatal asphyxia, shoulder dystocia, Apgar scores at 1 and 5 minutes and treatment and monitoring at the hospital. For most of the variables tested the risk of complications decreased with increasing PI. Thin newborn were thus at risk of having more complications than fat newborn. Only for shoulder dystocia the association was the divergent and having high PI, being short and fat, increased the risk of having shoulder dystocia at birth.

5.3 Relation between head circumference and health outcomes

When using χ^2 and Fisher's exact test, macrosomic newborns were grouped into three equal groups by head circumference; < 36cm, 36 - 36,9cm and ≥37cm, to compare variation in adverse birth outcomes with each of these head circumference categories (Table 8). As in analysis of birth length and outcome variables, only macrosomic newborns with BW above 4000g were chosen for these analyses. Chorioamnionitis, low Apgar score at 5 minute were left out from the outcome variables.

Of complications of birth, prolonged labor at second stage and unplanned caesarean section were significantly more common among macrosomic newborn having large head circumference than small head circumference. Only longer maternal hospital stay was associated with head circumference and different categories of head circumference differed statistically only for prevalence of perinatal asphyxia of newborn birth outcomes.

Table 8. Number and prevalence of birth outcome indicators in macrosomic newborns in three head circumference (HC) categories analysed with χ^2 test and Fisher's exact test.

	BW > 4000g						
	HC≤ 36,7cm (n=395)		HC 36,8 - 37,4cm (n=586)		HC ≥37,5cm (n=491)		
Complications of birth	n	%	n	%	n	%	*p*
Prolonged labor, 1st stage	20	5,1	17	2,9	17	3,5	*0,201*

Prolonged labor, 2nd stage	11	2,8	19	3,2	29	5,9	*0,030*
Caesarean section,unplanned	37	10,2	39	7,3	49	12,5	0,029
Maternal birth outcomes							
Hospital stay, ≥ 3 days	181	44,5	284	44,2	348	55,1	<0,001
Postpartum hemorrhage	37	9,4	53	9,0	40	8,1	0,795
Perineal trauma, 3rd or 4th degree	8	2,0	12	2,0	5	1,0	0,360
Using medical pain relief	336	85,1	492	84,0	395	80,4	0,146
Neonatal birth outcomes							
Perinatal asphyxia	21	5,3	24	4,1	42	8,6	0,007
Shoulder dystocia	2	0,5	1	0,2	5	1,0	0,168
Hypoglycemia	2	0,5	6	1,0	3	0,6	0,693
Chorioamnionitis	0	0	1	0,2	2	0,4	0,627
Low Apgar score 1min (≤6)	26	6,6	38	6,5	42	8,6	0,364
Low Apgar score 5min (≤6)	6	1,5	5	0,9	4	0,8	0,511
Treatment or monitoring at hospital	32	8,1	37	6,3	36	7,3	0,554

Association between birth length and birth outcomes was further studied with logistic regression analysis (Table 9). Increasing head circumference (HC) above smallest, reference category was associated with increasing the relative risk for prolonged labor at first stage and maternal postpartum hemorrhage. Whereas having HC in the highest category was associated with increased risk of prolonged labor at second stage, unplanned caesarean section, neonatal shoulder dystocia and low Apgar score at 1 minutes. Risk of longer maternal hospital stay and perinatal asphyxia was smaller and that of perineal trauma and the use of medical pain relief during labor bigger in newborn having head circumference in middle category compared with reference category. Head circumference had no significant association with the risk of hypoglycemia and treatment and monitoring at the hospital.

Table 9. Odds ratios, confidence intervals and p-values for outcome variables by three head circumference (HC) categories in macrosomic (>4000g) newborns. Smallest HC category is used as reference length.

Outcome variable	Head circumference category	OR	CI 95%	*p*
Prolonged labor 1st stage	< 36cm	1,0		
	36 – 36,9cm	2,361	1,459 – 3,822	< 0,001
	≥ 37cm	2,820	1,803 – 4,410	< 0,001
Prolonged labor 2nd stage	< 36cm	1,0		
	36 – 36,9cm	1,102	0,701 – 1,731	0,675
	≥ 37cm	1,856	1,292 – 2,668	0,001
Caesarean section, unplanned	< 36cm	1,0		
	36 – 36,9cm	1,005	0,737 – 1,370	0,974
	≥ 37cm	1,593	1,208 – 2,100	0,001
Maternal hospital stay	< 36cm	1,0		
	36 – 36,9cm	0,666	0,566 – 0,782	< 0,001
	≥ 37cm	1,028	0,874 – 1,210	0,736
Postpartum hemorrhage	< 36cm	1,0		
	36 – 36,9cm	1,778	1,358 – 2,328	< 0,001
	≥ 37cm	1,698	1,293 – 2,230	< 0,001
Perineal trauma, 3th or 4th degree	< 36cm	1,0		
	36 – 36,9cm	1,924	1,070 – 3,458	0,029
	≥ 37cm	0,723	0,293 – 1,785	0,482
Medical pain relief	< 36cm	1,0		
	36 – 36,9cm	1,431	1,152 – 1,777	0,001
	≥ 37cm	1,023	0,841 – 1,243	0,821
Perinatal asphyxia	< 36cm	1,0		
	36 – 36,9cm	0,524	0,348 – 0,788	0,002
	≥ 37cm	1,125	0,838 – 1,511	0,432
Shoulder dystocia	< 36cm	1,0		
	36 – 36,9cm	1,669	0,383 – 7,275	0,495
	≥ 37cm	4,984	1,944 – 12,780	0,001
Hypoglycemia	< 36cm	1,0		
	36 – 36,9cm	1,428	0,686 – 2,973	0,341
	≥ 37cm	1,412	0,678 – 2,941	0,356
Low Apgar score	< 36cm	1,0		

1min (≤6)	36 – 36,9cm	1,053	0,758 – 1,462	0,759
	≥ 37cm	1,457	1,093 – 1,943	0,010
Treatment or monitoring ICU	< 36cm	1,0		
	36 – 36,9cm	1,015	0,746 – 1,381	0,923
	≥ 37cm	1,143	0,853 – 1,531	0,370

Relation between head circumference and complications of birth and maternal and neonatal birth outcomes were further examined by creating a new composite variable body-brain ratio (BBR) to be analyzed with logistic regression analysis. As weight and length, also birth weight and head circumference correlates strongly with each other (R=0,648, p<0,001) and could not be used as individual variables in the analysis.

All outcome variables, except chorioamnionitis, prolonged labor at second stage and low Apgar score at 1 minute, were associated with body-brain proportionality (Table 10). The higher the BBR; larger proportion of the weight residing in the brain, the higher was the risk of experiencing perinatal asphyxia, hypoglycemia and caesarean section, having low Apgar score at 5 minute, ending up to treatment or monitoring at the hospital or longer hospital stay of the mother. Whereas for newborn having small BBR; small head for the other body, the risk of having shoulder dystocia, experiencing prolonged 2nd stage of labor, or mother experiencing complications, including hemorrhage, perineal trauma and using medical pain relief was larger than in newborn having larger head for the body.

Table 10. Logistic regression analyses of prevalence of outcome variables in relation to brain-body ratio (BBR), odds ratios (OR), confidence intervals (CI 95%) and p-values.

	OR	CI 95%	p
Perinatal asphyxia	1,465	1,359-1,579	<0,001
Shoulder dystocia	0,315	0,169-0,586	<0,001
Prolonged labor 1st stage	0,765	0,643-0,911	0,003
Prolonged labour 2nd stage	1,029	0,915-1,157	0,635
Caesarean section, unplanned	1,536	1,422-1,660	<0,001
Hospital stay mother	1,357	1,299-1,417	<0,001
Postpartum hemorrhage	0,771	0,706-0,841	<0,001

Perineal trauma, 3 or 4- degree	0,658	0,528-0,819	<0,001
Medical pain relief	0,792	0,755-0,832	<0,001
Hypoglycemia	1,560	1,291-1,886	<0,001
Chorioamniotitis	0,929	0,528-1,633	0,797
Apgar score 1min	1,070	0,978-1,170	0,142
Apgar score 5min	1,389	1,142-1,689	0,001
Treatment or monitoring ICU	1,095	1,006-1,192	0,036

6 DISCUSSION

The aim of this epidemiological study was to elucidate, whether obstetric and perinatal outcomes identified in earlier studies were associated with large birth weight also in data from Southwestern Finland. The objective was also to identify the role of other anthropometric parameters; birth length and head circumference for these adverse outcomes for the mother and newborn. This study was based on data from the Finnish Medical Birth Register from Southwestern Finland during the period 2008 – 2010.

The prevalence of macrosomia, defined as BW > 4000g was found to be 18%. In nationwide data from year 2010, the percentage of macrosomic newborn was 16,7% and there has been steady decline in the rate of newborn macrosomia over the last two decades (Vuori and Gissler, 2011). There has been debate about appropriate weight limit for macrosomia, since in earlier studies the risk of adverse birth outcome has been found to increase sharply with newborn weight above 4500g and this has been suggested to be a better predictor of morbidity (Bjorstad et al., 2010; Boulet et al., 2003; Das et al., 2009). Also in our data, the rate of many birth outcome indicators increased by increasing weight above 4500g. However differences in the rates of indicators were not substantial and the small amount of newborn with BW above 4500g (n=261) prevented more detailed analysis. On the other hand, increase in birth weight related morbidity has been shown to start already at 3500g and continue to increase as birth weight increases (Stotland et al., 2004). Thus examining morbidity associated with macrosomia across different birth weight thresholds could have resulted in different results.

The proportion of adverse outcomes attributable to macrosomia ranged from 62.5% of all cases of shoulder dystocia to 14.9% of all cases of perinatal asphyxia. Prolonged labor cannot be defined as adverse outcome of birth itself, but a contributor for maternal birth complications and thus was selected as an indicator for our study. Prolonged second stage of labor has been shown to occur more often with macrosomic than with normal weight newborn (Boulet et al., 2003; Karimu et al., 2003), which is consistent also with our data and we found also prolonged labor at first stage to be associated with macrosomia. Similarly, the use of pharmacological methods for a pain relief during the labor cannot be defined as adverse outcome of the birth, although some adverse effects of using pharmacological pain relief has been reported (Jones et al., 2012). Macrosomia was found to be associated with prolonged labor at first and second stage of labor, unplanned caesarean section, postpartum hemorrhage, the use of medical pain relief during labor, perinatal asphyxia, shoulder dystocia, Apgar score at 1 minutes and admission to treatment of monitoring at ICU or another hospital ward, as in previous studies (Bjorstad et al., 2010; Ju et al., 2009; Linder et al., 2014; Weissmann-Brenner et al., 2012). Linder et al. (2014) found also higher rates of hypoglycemia among macrosomic newborn than normal weight newborn, but in our data significant difference in hypoglycemia rates was only found between AGA and LGA newborns (0,7% vs. 3.6%, $p<0,001$), not by comparing macrosomic and normal weight newborns. This may be due to differences in the definition of hypoglycemia or differences in management of maternal diabetes, since it is in most cases the underlying cause for neonatal hypoglycemia. Also chorioamnionitis (Stotland et al., 2004) and Apgar score at 5 minutes (Boulet et al., 2003) has been linked with macrosomia, but we found no such association.

It was discovered that birth length is associated with higher prevalence and risk for macrosomia related morbidity. To our knowledge no previous study has reported this phenomenon. Previously, birth length has been found to have an independent effect on perinatal mortality, however morbidity was not reported in this study (Melve et al., 2000). In this study, there was only few neonatal deaths in the data and the association found by Melve et al. (2000), could not be confirmed. Birth length and head circumference has been used previously in indices, such as weight to length ratio, PI or midarm circumference to head circumference ratio, when studying the association between newborn body proportionality and birth outcome (Bertagnon et al., 2003; Patterson and Pouliot, 1987; Persson et al., 2012), but with conflicting results. In some of the previous studies PI, weight for length or body proportionality measured by PI percentiles ratio has been associated with perinatal morbidity (Bertagnon et al., 2003; Bollepalli et al., 2010; Patterson and Pouliot, 1987), but in more recent study by Persson et al. (2012) there was no difference in risk for morbidity between proportionate and disproportionate LGA newborn. In study by Bollepalli et al. (2010) symmetric LGA newborn with high PI were at higher risk for hypoglycemia, hyperbilirubinemia, acidosis and composite morbidity. High PI stands for fatter and shorter babies and thus these findings were not consistent with this study, since we found rate of morbidity to increase by increasing height and the risk for morbidity indicators, except for shoulder dystocia risk to decrease by increasing PI. This could be due to differences in study design and outcome variables studied. However more studies are needed on the subject to confirm, which of the anthropometric measurements are important determinants for birth outcomes.

The association between head circumference and birth outcome has been studied sparsely. Usefulness of composite indices of mid-arm circumference / head circumference ratio has been studied in the 80’s and 90’s at some extent and one study found it to be more sensitive than birth weight in distinguishing symptomatic LGA newborn from asymptomatic newborn born to diabetic mothers (Georgieff et al., 1986). Head circumference as a single measure has been associated with labor complications, such as cesarean section, vacuum-assisted and forceps-assisted vaginal delivery and maternal and fetal distress (Elvander et al., 2012; Kennelly et al., 2003; Mujugira et al., 2013). Results of this study support these findings, since we also found all labor complications to be associated with head circumference in macrosomic newborn and the risk for labor complications increased with increasing head circumference. Interestingly new finding in this study was that also some maternal and newborn birth outcome indicators were associated with head circumference. The risks for postpartum hemorrhage, shoulder dystocia and low Apgar score at 1 minute were increased with increasing head circumference, whereas risks for longer maternal hospital stay and perinatal asphyxia were smallest in the average group of head circumference.

Birth length and head circumference are associated with short-term birth outcomes for both mother and newborn. In our study birth length and head circumference was measured after birth, in retrospect to birth complications. However our results enhance our understanding on the association between newborn anthropometric measures and the birth outcome and may help to develop new methods to diagnose and manage macrosomia already in fetal period.

This study has certain limitations as well as some strength. Regarding the latter, the data in our study was from nationwide register, which has been proven for its reliability and accuracy (Gissler and Shelley, 2002; Gissler et al., 1995). We had also data from all children from two years period from one of the largest regions in the country, improving generalization of the results for the whole country. In this study, association of size of birth with many different birth outcome indicators was studied, which can be considered also strength of this study. However relatively low number of cases in our data can be considered also a limitation, since there were only limited amount of macrosomic newborn in the data, which impacted the selection of data analysis methods. The register data was also limited to the time, newborn and mothers stayed in the hospital and thus long term effects of size of birth could not be studied.

7 CONCLUSION

In conclusion birth length and head circumference were associated with many birth outcome variables in macrosomic infants, usually linked in literature often only with high birth weight. The results suggest length and head circumference would be valuable additional predictors with birth weight, when evaluating perinatal morbidity risk.

8 REFERENCES

AAP (American Academy of Pediatrics), Committee on Fetus and Newborn. Age terminology during the perinatal period. Pediatrics. 2004, 114(5):1362-4.

Abel EL. Smoking during pregnancy: a review of effects on growth and development of offspring. Hum Biol. 1980, 52(4):593-625.

Abrams B, Selvin S. Maternal weight gain pattern and birth weight. Obstet Gynecol 1995, 86:163–9.

Araújo CL, Hallal PC, Nader GA, Menezes AM, Victora CG. Size at birth and height in early adolescence: a prospective birth cohort study. Cad Saude Publica. 2008, 24(4):871-8.

Baird, J., D. Fisher, P. Lucas, J. Kleijnen, H. Roberts, and C. Law. Being big or growing fast: systematic review of size and growth in infancy and later obesity. BMJ, 2005, 331 (7522): 929.

Baker JL, Olsen LW, Sørensen T. Weight at birth and all-cause mortality in adulthood. Epidemiology. 2008, 19(2):197-203.

Bamfo J and Obido A. Diagnosis and Management of Fetal Growth Restriction. J Pregnancy. 2011: 640715. doi: 10.1155/2011/640715.

Basavanthappa BT. Textbook of Midwifery & Reproductive Health Nursing. Jaypee Brothers Medical Publishers ltd. 2006, India.

Basso O, Wilcox AJ, Weinberg CR. Birth weight and mortality: causality or confounding? Am J Epidemiol. 2006, 164:303–311.

Bernstein IM, Mongeon JA, Badger GJ, Solomon L, Heil SH, Higgins ST. Maternal smoking and its association with birth weight. Obstet Gynecol. 2005, 106(5 Pt 1):986-91.

Bertagnon, JR., de Mattos Segre CA, and Dall Colletto GM. Weight-for-length relationship at birth to predict neonatal diseases: Sao Paulo Med J. 2003, 121: 149-54.

Bjorstad AR, Irgens-Hansen K, Daltveit AK, and Irgens LM. Macrosomia: mode of delivery and pregnancy outcome: Acta Obstet Gynecol Scand. 2010, 89: 664-9.

Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, Mathers C, Rivera J; Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: global and regional exposures and health consequences. Lancet. 2008, 371(9608):243-60.

Bollepalli S, Dolan LM, Miodovnik M, Feghali M and Khoury JC. Asymmetric large-for-gestational-age infants of type 1 diabetic women: morbidity and abdominal growth: Am J Perinatol. 2010, 27: 603-10.

Boulet SL, Alexander GR, Salihu HM, et al. Macrosomic births in the United States—determinants, outcomes, and proposed grades of risk. Am J Obstet Gynecol. 2003, 188:1372–1378.

Broekman BF, Chan YH, Chong YS, Quek SC, Fung D, Low YL, Ooi YP, Gluckman PD, Meaney MJ, Wong TY, Saw SM. The influence of birth size on intelligence in healthy children. Pediatrics. 2009, 123(6):e1011-6.

Brosco JP, Sanders LM, Guez G, Lantos JD. Historical trends in low birth weight. Arch Pediatr Adolesc Med. 2010, 164(1):99-100.

Brown JE, Murtaugh MA, Jacobs DR Jr, Margellos HC. Variation in newborn size according to pregnancy weight change by trimester. Am J Clin Nutr. 2002, 76(1):205-9.

Camilleri AP and Cremona V. The effect of parity on birth weight. BJOG, 1970, 77(2); 145-147.

Chatfield J. ACOG Issues Guidelines on Fetal Macrosomia. Am Fam Physician. 2001, 64(1):169-170.

Chike-Obi U, David RJ, Coutinho R, Wu SY. Birth weight has increased over a generation. Am J Epidemiol. 1996, 144(6):563-9.

Clausson B, Lichtenstein P and Cnattingius S. Genetic influence on birthweight and gestational length determined by studies in offspring of twins. BJOG. 2000, 107(3):375-81.

Crane JM, White J, Murphy P, Burrage L, Hutchens D. The effect of gestational weight gain by body mass index on maternal and neonatal outcomes. J Obstet Gynaecol Can. 2009, 31(1):28-35.

Das S, Irigoyen M, Patterson MB, Salvador A and Schutzman DL. Neonatal outcomes of macrosomic births in diabetic and non-diabetic women: Arch Dis Child Fetal Neonatal Ed. 2009, 94: F419-22.

Diamond I, McDonald J and Guidotti R. Use of a simple anthropometric measure to predict birth weight. Bulletin of the World Health Organization. 1993; 71(2): 157-163.

Djelmis J, Buković D, Pfeifer D, Ivanisević M. Ponderal index and disproportionate fetal growth in IDDM pregnancies. Coll Antropol. 1998, 22(2):491-5.

Dunkel L. Inuterine growth – Normal growth – Pediatrics in Duodecim textbooks, 1.5.2010. http://www.terveysportti.fi/dtk/oppi/koti?p_artikkeli=lta00041&p_haku=syntym%C3%A4paino, viewed 5.5.2013.

Elshibly EM, Schmalisch G. The effect of maternal anthropometric characteristics and social factors on gestational age and birth weight in Sudanese newborn infants. BMC Public Health. 2008, 18;8:244.

Elvande C, Hogberg U and Ekeus C. The influence of fetal head circumference on labor outcome: a population-based register study: Acta Obstet Gynecol Scand. 2012, 91: 470-5.

Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, Bauer CR, Donovan EF, Korones SB, Laptook AR, Lemons JA, Oh W, Papile LA, Shankaran S, Stevenson DK, Tyson JE, Poole WK; NICHD Neonatal Research Network. Trends in neonatal morbidity and mortality for very low birthweight infants. Am J Obstet Gynecol. 2007, 196(2):147.e1-8.

Fay RA, Dey PL, Saadie CM, Buhl JA, Gebski VJ. Ponderal index: a better definition of the 'at risk' group with intrauterine growth problems than birth-weight for gestational age in term infants. Aust N Z J Obstet Gynaecol. 1991, 31(1):17-9.

Feleke Y, Enquoselassie F. Maternal age, parity and gestational age on the size of the newborn in Addis Ababa. East Afr Med J. 1999, 76(8):468-71.

Friedlander Y, Manor O, Paltiel O, Meiner V, Sharon N, Calderon R, Hochner H, Sagy Y, Avgil M, Harlap S, Siscovick DS. Birth weight of offspring, maternal pre-pregnancy characteristics, and mortality of mothers: the Jerusalem perinatal study cohort. Ann Epidemiol. 2009, 19(2):112-7.

Gage TB, Fang F, O'Neill E, Stratton H. Maternal age and infant mortality: a test of the Wilcox-Russell hypothesis. Am J Epidemiol. 2009, 1;169(3):294-303.

Georgieff MK, Sasanow SR, Mammel MC and Pereira GR. Mid-arm circumference/head circumference ratios for identification of symptomatic LGA, AGA, and SGA newborn infants: J Pediatr. 1986, 109: 316-21.

Gielen M, Lindsey PJ, Derom C, Smeets HJ, Souren NY, Paulussen AD, Derom R, Nijhuis JG. Modeling Genetic and Environmental Factors to Increase Heritability and Ease the Identification of Candidate Genes for Birth Weight: A Twin Study. Behav Genet. 2008, 38(1): 44–54.

Gissler M and Shelley J. Quality of data on subsequent events in a routine Medical Birth Register: Med Inform Internet Med. 2002, 27: 33-8.

Gissler M, Teperi J, Hemminki E and Merilainen J. Data quality after restructuring a national medical registry: Scand J Soc Med. 1995, 23: 75-80.

Graafmans WC, Richardus JH, Borsboom GJ, Bakketeig L, Langhoff-Roos J, Bergsjø P, Macfarlane A, Verloove-Vanhorick SP, Mackenbach JP; EuroNatal working group. Birth weight and perinatal mortality: a comparison of "optimal" birth weight in seven Western European countries. Epidemiology. 2002, 13(5):569-74.

Haas JD, Moreno-Black G, Frongillo EA Jr, Pabon J, Pareja G, Ybarnegaray J, Hurtado L. Altitude and infant growth in Bolivia: a longitudinal study. Am J Phys Anthropol. 1982 Nov;59(3):251-62.

Haavaldsen C, Samuelsen SO and Eskild A. Fetal death and placental weight/birthweight ratio: a population study. Acta Obstetricia et Gynecologica Scandinavica. 2013, 92(5); 583–590.

Hack M, Schluchter M, Cartar L, Rahman M, Cuttler L, Borawski E. Growth of very low birth weight infants to age 20 years. Pediatrics. 2003;112(1).

Hadfield RM, Lain SJ, Simpson JM, Ford JB, Raynes-Greenow CH, Morris JM, Roberts CL. Are babies getting bigger? An analysis of birthweight trends in New South Wales, 1990-2005. Med J Aust. 2009, 190(6):312-5.

Hafner E, Schuchter K, Metzenbauer M, Philipp K. Uterine artery Doppler perfusion in the first and second pregnancies. Ultrasound Obstet Gynecol. 2000, 16(7):625-9.

Harding S, Boroujerdi M, Santana P and Cruickshank JK. Decline in, and lack of difference between, average birth weights among African and Portuguese babies in Portugal. Int J Epidemiol. 2006, 35(2): 270-276.

Hartinger S, Tapia V, Carrillo C, Bejarano L, Gonzales GF. Birth weight at high altitudes in Peru. Int J Gynaecol Obstet. 2006, 93(3):275-81.

Hediger ML, Overpeck MD, Maurer KR, Kuczmarski RJ, McGlynn A, Davis WW. Growth of infants and young children born small or large for gestational age: findings from the Third National Health and Nutrition Examination Survey. Arch Pediatr Adolesc Med. 1998, 152(12): 1225-31.

Hemachandra AH, Klebanoff MA, Duggan AK, Hardy JB, Furth SL. The association between intrauterine growth restriction in the full-term infant and high blood pressure at age 7 years: results from the Collaborative Perinatal Project. Int J Epidemiol. 2006, 35(4):871-7.

Henriksen T. The macrosomic fetus: a challenge in current obstetrics. Acta Obstet Gynecol Scand 2008; 87: 134-145.

Hernández-Díaz S, Schisterman EF, Hernán MA. The birth weight "paradox" uncovered? Am J Epidemiol. 2006, 1;164(11):1115-20.

Hop le T. Secular trend in size at birth of Vietnamese newborns during the last 2 decades (1980-2000). Asia Pac J Clin Nutr. 2003, 12(3):266-70.

ICD-10 Tautiluokitus. 1999. Suomalainen 2. uudistettu painos Maailman terveysjärjestön (WHO) luokituksesta ICD-10. Sosiaali- ja terveysalan tutkimus- ja kehittämiskeskus. Helsinki: STAKES.

ICD-10, Version 2010: http://apps.who.int/classifications/icd10/browse/2010/en#/P08.0, viewed 6 of Nov 2012.

Itani O, Niedbala B, Tsang R. Small-for-Gestational-Age Infant and Problems of Prematurity, in *Pediatric Nutrition in Chronic Diseases and Developmental Disorders*, second edition, 2005, Oxford University Press, New York.

Jones, L., M. Othman, T. Dowswell, Z. Alfirevic, S. Gates, M. Newburn, S. Jordan, T. Lavender, and J. P. Neilson, 2012, Pain management for women in labour: an overview of systematic reviews: Cochrane Database Syst Rev, v. 3, p. Cd009234.

Ju H, Chadha Y, Donovan T and O'Rourke P. Fetal macrosomia and pregnancy outcomes. Aust N Z J Obstet Gynaecol. 2009, 49: 504-9.

Julian CG, Hageman JL, Wilson MJ, Vargas E, Moore LG. Lowland origin women raised at high altitude are not protected against lower uteroplacental O2 delivery during pregnancy or reduced birth weight. Am J Hum Biol. 2011, 23(4): 509-16.

Kajantie E, Osmond C, Barker DJ, Forsén T, Phillips DI and Eriksson JG. Size at birth as a predictor of mortality in adulthood: a follow-up of 350 000 person-years. Int J Epidemiol. 2005, 34:655–663.

Kandraju H, Agrawal S, Geetha K, Sujatha L, Subramanian S, Murki S. Gestational age-specific centile charts for anthropometry at birth for South Indian infants. Indian Pediatr. 2012, 49(3):199-202.

Karimu AL, Ayoade G and Nwebube NI. Arrest of descent in second stage of labour secondary to macrosomia: a case report: J Obstet Gynaecol Can. 2003, 25: 668-70.

Karvonen M, Hannila ML, Saari A, Dunkel L. New Finnish reference for head circumference from birth to 7 years. Ann Med. 2012, 44(4):369-74.

Kennelly MM, Anjum R, Lyons S and Burke G. Postpartum fetal head circumference and its influence on labour duration in nullipara: J Obstet Gynaecol. 2003, 23: 496-9.

Klebanoff MA, Mednick BR, Schulsinger C, Secher NJ, Shiono PH. Father's effect on infant birth weight. Am J Obstet Gynecol. 1998, 178(5):1022-6.

Klebanoff MA, Yip R. Influence of maternal birth weight on rate of fetal growth and duration of gestation. J Pediatr. 1987, 111(2):287-92.

Knight B, Shields BM, Turner M, Powell RJ, Yajnik CS, Hattersley AT. Evidence of genetic regulation of fetal longitudinal growth. Early Hum Dev. 2005, 81(10):823-31.

Koyanagi A, Zhang J, Dagvadorj A, Hirayama F, Shibuya K, Souza JP, Gülmezoglu AM. Macrosomia in 23 developing countries: an analysis of a multicountry, facility-based, cross-sectional survey. Lancet. 2013, 381(9865):476-83.

LabSpace, Open Learn. 7.3.2 The mid upper arm circumference, http://labspace.open.ac.uk/mod/oucontent/view.php?id=452813&section=1.5.2, viewed 3.6.2013.

Lagström, H., P. Rautava, A. Kaljonen, H. Räihä, P. Pihlaja, P. Korpilahti, V. Peltola, P. Rautakoski, E. Osterbacka, O. Simell, and P. Niemi, 2012, Cohort Profile: Steps to the Healthy Development and Well-being of Children (the STEPS Study): Int J Epidemiol. 2013, 42(5): 1273-84.

Leonardi-Bee J, Smyth A, Britton J, Coleman T. Environmental tobacco smoke and fetal health: systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2008, 93(5): F351-61.

Lepercq J, Lahlou N, Timsit J, Girard J, Mouzon SH. Macrosomia revisited: ponderal index and leptin delineate subtypes of fetal overgrowth. Am J Obstet Gynecol. 1999, 181(3): 621-5.

Linder N, Lahat Y, Kogan A, Fridman E, Kouadio F, Melamed N, Yogev Y and Klinger G. Macrosomic newborns of non-diabetic mothers: anthropometric measurements and neonatal complications: Arch Dis Child Fetal Neonatal Ed. 2014, 99: F353-8.

Lindqvist PG, Molin J. Does antenatal identification of small-for-gestational age fetuses significantly improve their outcome? Ultrasound Obstet Gynecol. 2005, 25(3):258.

Lu Y, Zhang J, Lu X, Xi W, Li Z. Secular trends of macrosomia in southeast China, 1994-2005. BMC Public Health. 2011, Oct 20;11:818. doi: 10.1186/1471-2458-11-818.

Lunde A, Melve KK, Gjessing HK, Skjaerven R, Irgens LM. Genetic and Environmental Influences on Birth Weight, Birth Length, Head Circumference, and Gestational Age by Use of Population-based Parent-Offspring Data. Am. J. Epidemiol. 2007, 165(7): 734-41.

Lönnqvist T, Mäki P and Salo J. Head circumference, in *Health inspections in child health clinics and school health care, method hand book* (in finnish, Päänympärys, Terveystarkastukset lastenneuvolassa ja kouluterveydenhuollossa, menetelmäkäsikirja), Finnish National Institute for Health and Welfare, 2011, Tampere.

Magnus P: Causes of variation in birth weight: a study of offspring of twins. Clin Genet. 1984, 25*:* 15–24.

Marconi AM, Ronzoni S, Bozzetti P, Vailati S, Morabito A, and Battaglia FC. Comparison of fetal and neonatal growth curves in detecting growth restriction. Obstetrics and Gynecology. 2008, 112(6), 1227–34.

McLennan JE, Gilles FH, Neff RK. A model of growth of the human fetal brain. In: Gilles FH, Leviton A, Dooling EC, eds. *The developing human brain: growth and epidemiologic neuropathy*. Boston, MA: Wright P G, 1983:43–58.

The Monitoring and Evaluation to Assess and Use Results Demographic and Health Surveys (Measure DHS). Quality information to plan,monitor, and improve population, health, and nutrition programs, http://www.measuredhs.com/Who-We-Are/About-Us.cfm, viewed 3.6.2013.

Mehta S, Tandon A, Dua T, Kumari S, Singh SK. Clinical assessment of nutritional status at birth. Indian Pediatr. 1998, 35(5):423-8.

Melve KK, Gjessing HK, Skjaerven R and Oyen N. Infants' length at birth: an independent effect on perinatal mortality: Acta Obstet Gynecol Scand. 2000, 79: 459-64.

Meyer MB, Comstock GW. Maternal cigarette smoking and perinatal mortality. Am J Epidemiol. 1972, 96(1):1-10.

Miller HC, Hassanein K. Diagnosis of impaired fetal growth in newborn infants. Pediatrics. 1971, 48(4):511-22.

Mirmiran P, Moslehi N, Asghari G, Jambarsang S, Mehrabi Y, Azizi F. Secular trends in size at birth of Iranian neonates: meta-analyses of published and unpublished studies. Ann Hum Biol. 2013, 40(1):75-82.

Mironov B. Birth weight and physical stature in St. Petersburg: living standards of women in Russia, 1980-2005. Econ Hum Biol. 2007, 5(1):123-43.

Misra DP, Astone N, Lynch CD. Maternal smoking and birth weight: interaction with parity and mother's own in utero exposure to smoking. Epidemiology. 2005, 16(3):288-93.

Mook-Kanamori DO, van Beijsterveldt CE, Steegers EA, Aulchenko YS, Raat H, Hofman A, Eilers PH, Boomsma DI, Jaddoe VW. Heritability estimates of body size in fetal life and early childhood. PLoS One. 2012, 7(7):e39901.

Moore LG. Comparative human ventilatory adaptation to high altitude. Respir Physiol. 2000, 121*:* 257–276.

Mujugira A, Osoti A, Deya R, Hawes SE and Phipps AI. Fetal head circumference, operative delivery, and fetal outcomes: a multi-ethnic population-based cohort study: BMC Pregnancy Childbirth. 2013, 13: 106.

Nahar S, Mascie-Taylor CG, Begum HA. Maternal anthropometry as a predictor of birth weight. Public Health Nutr. 2007, 10(9):965-70.

Ng S-K, Olog A, Spinks AB, Cameron CM, Searle J, and McClure RJ. Risk factors and obstetric complications of large for gestational age births with adjustments for community effects: results from a new cohort study. BMC Public Health. 2010; 10: 460.

Noeker M: Neurocognitive development in children experiencing intrauterine growth retardation and born small for gestational age: pathological, constitutional and therapeutic pathways. Horm Res 2005;64(suppl 3):83–88.

OECD. “Infant health”, in *Society at a Glance* 2009: OECDSocial Indicators, OECD Publishing, 2009. http://dx.doi.org/10.1787/soc_glance-2008-24-en

OECD. Health at glance: Europe 2012, Health status, Infant health: low birth weight. http://www.oecd-ilibrary.org/sites/9789264183896-en/01/09/g1-09-01.html?contentType=&itemId=/content/chapter/9789264183896-12-en&containerItemId=/content/serial/23056088&accessItemIds=/content/book/9789264183896-en&mimeType=text/html, viewed 3.6.2013.

Oishi K, Honda S, Takamura N, Kusano Y, Abe Y, Moji K, Takemoto T, Tahara Y, Aoyagi K. Secular trends of sizes at birth in Japanese healthy infants born between 1962 and 1988. J Physiol Anthropol Appl Human Sci. 2004, 23(5):155-61.

Olsen IE, Groweman SA, Lawson L, Clark RH, Zemel B. New Intrauterine Growth Curves Based on United States Data. Pediatrics. 2010, 125(2); e214 -e224.

Ong KK, Preece MA, Emmett PM, Ahmed ML, Dunger DB. Size at birth and early childhood growth in relation to maternal smoking, parity and infant breast-feeding: longitudinal birth cohort study and analysis. Pediatr Res. 2002, 52: 863–867.

de Onis M, Blössner M, Villar J. Levels and patterns of intrauterine growth retardation in developing countries. Eur J Clin Nutr. 1998, 52(Suppl 1): S5-15.

Ott WJ. The diagnosis of altered fetal growth. Obstet Gynecol Clin North Am. 1988, 15:237–63.

Park S, Sappenfield WM, Bish C, Salihu H, Goodman D, Bensyl DM. Assessment of the Institute of Medicine recommendations for weight gain during pregnancy: Florida, 2004-2007. Matern Child Health J. 2011, 15(3):289-301.

Patterson RM and Pouliot MR. Neonatal morphometrics and perinatal outcome: who is growth retarded? Am J Obstet Gynecol. 1987, 157: 691-3.

Peleg D, Kennedy CM and Hunter SK. Intrauterine Growth Restriction: Identification and Management. Am Fam Physician. 1998, 58(2):453-460.

Persson M, Pasupathy D, Hanson U and Norman M. Disproportionate body composition and perinatal outcome in large-for-gestational-age infants to mothers with type 1 diabetes: BJOG. 2012, 119: 565-72.

Pickett KE, Abrams B, Selvin S. Maternal height, pregnancy weight gain, and birthweight. Am J Hum Biol. 2000, 12(5):682-687.

Pietiläinen KH, Kaprio J, Räsänen M, Winter T, Rissanen A, Rose RJ. Tracking of body size from birth to late adolescence: contributions of birth length, birth weight, duration of gestation, parents' body size, and twinship. Am J Epidemiol. 2001, 1;154(1):21-9.

Pihkala J, Hakala T, Voutilainen P and Raivio K. Characteristic of recent fetal growth curves in Finland (in finnish). Duodecim 1989, 105:1540-6.

Primhak RA, MacGregor DF. Ethnic and environmental factors affecting fetal growth in Papua New Guinea. Ann Hum Biol. 1991, 18(3):235-43.

Pulver LS, Guest-Warnick G, Stoddard GJ, Byington CL and Young PC. Weight for gestational age affects the mortality of late preterm infants: Pediatrics. 2009, 123: e1072-7.

Raio L, Ghezzi F, Di Naro E, Buttarelli M, Franchi M, Dürig P and Brühwiler H. Perinatal outcome of fetuses with a birth weight greater than 4500 g: an analysis of 3356 cases. Eur J Obstet Gynecol Reprod Biol. 2003, 109: 160-5.

Rasmussen KM, Yaktine AL (ed.) Institute of Medicine (Committee to Reexamine IOM Pregnancy Weight Guidelines, Food and Nutrition Board and Board on Children, Youth and Families). Weight gain During Pregnancy: Reexamining the Guidelines. Washington DC: National Academy Press, 2009.

Rice F and Thapar A. Estimating the relative contributions of maternal genetic, paternal genetic and intrauterine factors to offspring birth weight and head circumference. Early Hum Dev. 2010, 86(7): 425–432.

Rode L, Hegaard HK, Kjaergaard H, Møller LF, Tabor A, Ottesen B. Association between maternal weight gain and birth weight. Obstet Gynecol. 2007, 109(6):1309-15.

Rogers JM. Tobacco and pregnancy: overview of exposures and effects. Birth Defects Res C Embryo Today. 2008, 84(1):1-15.

Roland MCP, Friis CM, Voldner N, Godang K, Bollerslev J, Haugen G and Henriksen T. Fetal Growth versus Birthweight: The Role of Placenta versus Other Determinants. PLoS One. 2012, 7(6): e39324. doi:10.1371/journal.pone.0039324

Ross JA. High birthweight and cancer: evidence and implications. Cancer Epidemiol Biomarkers Prev. 2006, 15: 1-2.

Rossi AC, Mullin P and Prefumo F. Prevention, Management, and Outcomes of Macrosomia: A Systematic Review of Literature and Meta-analysis. Obstet Gynecol Surv. 2013. 68: 702-9.

Rosso P. Morbidity and mortality in intrauterine growth retardation, in *Intrauterine Growth Retardation*. Nestlé Nutrition Workshops Series, Vol. 18, New York: Raven Press, 1989.

Saenger P, Czernichow P, Hughes I, Reiter EO: Small for gestational age: short stature and beyond. Endocr Rev 2007, 28:219–251.

Salafia CM, Zhang J, Miller RK, Charles AK, Shrout P, Sun W. Placental growth patterns affect birth weight for given placental weight. Birth Defects Res A Clin Mol Teratol. 2007, 79(4):281-8.

Salo J, Mäki P and Dunkel L. Weight, in *Health inspections in child health clinics and school health care, method hand book* (in finnish, Weight, Terveystarkastukset lastenneuvolassa ja kouluterveydenhuollossa, menetelmäkäsikirja, Finnish National Institute for Health and Welfare, 2011, Tampere.

Salo J, Mäki P and Dunkel L. Length / Height. in *Health inspections in child health clinics and school health care, method hand book* (in finnish, Päänympärys, Terveystarkastukset lastenneuvolassa ja kouluterveydenhuollossa, menetelmäkäsikirja), Finnish National Institute for Health and Welfare, 2011, Tampere.

Sanin LH, López SR, Olivares ET, Terrazas MC, Silva MA, Carrillo ML. Relation between birth weight and placenta weight. Biol Neonate. 2001, 80(2):113-7.

Sankilampi U, Hannila ML, Saari A, Gissler M and Dunkel L. New population-based references for birth weight, length, and head circumference in singletons and twins from 23 to 43 gestation weeks. Ann Med. 2013, 45: 446-54.

Sauerborn R, Ouiminga RM, Koné B, Sama R, Oepen C, Ebrahim GJ. Neonatal mid-upper-arm circumference is a valid proxy for birth-weight. Trop Med Parasitol. 1990; 41(1):65-7.

Schell LM, Hodges DC. Variation in size at birth and cigarette smoking during pregnancy. Am J Phys Anthropol. 1985, 68(4):549-54.

Sekiya N, Anai T, Matsubara M, Miyazaki F. Maternal weight gain rate in the second trimester are associated with birth weight and length of gestation. Gynecol Obstet Invest. 2007;63(1):45-8.

Shah PS; Knowledge Synthesis Group on Determinants of LBW/PT births. Parity and low birth weight and preterm birth: a systematic review and meta-analyses. Acta Obstet Gynecol Scand. 2010, 89(7):862-75.

Shehata F, Levin I, Shrim A, Ata B, Weisz B, Gamzu R, Almog B. Placenta/birthweight ratio and perinatal outcome: a retrospective cohort analysis. BJOG. 2011, 118(6):741-7.

Siervo M, Horta BL, Stephan BC, Victora CG, Wells JC. First-borns carry a higher metabolic risk in early adulthood: evidence from a prospective cohort study. PLoS One. 2010, 9;5(11):e13907.

Spencer N, Bambang S, Logan S and Gill L. Socioeconomic status and birth weight: comparison of an area-based measure with the Registrar General's social class. J Epidemiol Community Health. 1999, 53:495-498 doi:10.1136/jech.53.8.495

Stamnes Koepp UM, Frost Andersen L, Dahl-Joergensen K, Stigum H, Nass O, Nystad W. Maternal pre-pregnant body mass index, maternal weight change and offspring birthweight. Acta Obstet Gynecol Scand. 2012, 91(2):243-9.

De Stavola BL, Leon DA, Koupil I. Intergenerational correlations in size at birth and the contribution of environmental factors: The Uppsala Birth Cohort Multigenerational Study, Sweden, 1915-2002. Am J Epidemiol. 2011, 174(1):52-62.

Steckel RH. Birth weights and stillbirths in historical perspective. Eur J Clin Nutr. 1998, 52(Sl) 1:S16-20.

Stein AD, Lumey LH. The relationship between maternal and offspring birth weights after maternal prenatal famine exposure: the Dutch Famine Birth Cohort Study. Hum Biol. 2000, 72(4):641-54.

Stein ZA, Susser M. Intrauterine growth retardation: epidemiological issues and public health significance. Semin Perinatol. 1984, 8(1):5–14.

Stephens MB, Manning DA, Arnold-Canuso A, Haas DM. Maternal shoe size and infant birth weight: correlation or fiction? J Am Board Fam Med. 2006, 19(4):426-8.

Stotland, N. E., A. B. Caughey, E. M. Breed, and G. J. Escobar, 2004, Risk factors and obstetric complications associated with macrosomia: Int J Gynaecol Obstet, v. 87, p. 220-6.

Strauss RS, Dietz WH. Low maternal weight gain in the second or third trimester increases the risk for intrauterine growth retardation. J Nutr. 1999, 129:988–93.

Surkan PJ, Hsieh CC, Johansson AL, Dickman PW, Cnattingius S. Reasons for increasing trends in large for gestational age births. Obstet Gynecol. 2004, 104(4):720-6.

Swamy GK, Edwards S, Gelfand A, James SA, Miranda ML. Maternal age, birth order, and race: differential effects on birthweight. J Epidemiol Community Health. 2012, 66(2):136-42.

Teperi J. Multi method approach to the assessment of data quality in the Finnish Medical Birth Registry. J Epidemiol Community Health. 1993, 47: 242-7.

Teramo K. Sikiön makrosomia on yhä äidin diabeteksen suuri ongelma. Lääketieteellinen Aikakauskirja Duodecim, 1998, 114(21):2253.

Thame M, Osmond C, Trotman H. Fetal growth and birth size is associated with maternal anthropometry and body composition. Matern Child Nutr. 2012, Dec 13. doi: 10.1111/mcn.12027.

THL, National Institute for Health and Welfare. Lasten kasvunseurannan uudistaminen, Asiantuntijaryhmän raportti. 49/2011, Tampere, http://www.thl.fi/thl-client/pdfs/d721d127-0123-4cea-a5a1-c3cba87d6722, viewed 15.5.2014

THL, National Institute for Health and Welfare. 3rd edition of the Finnish version of the the International Statistical Classification of Diseases and Related Health Problems (ICD-10), 5/2011. http://www.thl.fi/thl-client/pdfs/15c30d65-2b96-41d7-aca8-1a05aa8a0a19, viewed 2.9.2014.

Tiitinen A. Raskaus ja tupakointi. Lääkärikirja Duodecim, Terveyskirjasto, 21.9.2012. http://www.terveyskirjasto.fi/terveyskirjasto/tk.koti?p_artikkeli=dlk00984

Tuvemo T, Cnattingius S and Jonsson B. Prediction of Male Adult Stature Using Anthropometric Data at Birth: A Nationwide Population-Based Study. Pediatric Research. 1999, 46; 491–491.

United Nations Children’s Fund and World Health Organization (UNICEF & WHO). Low Birthweight: Country, regional and global estimates. UNICEF, New York, 2004. http://whqlibdoc.who.int/publications/2004/9280638327.pdf, viewed 15.9.2014.

Veena SR, Krishnaveni GV, Wills AK, Kurpad AV, Muthayya S, Hill JC, Karat SC, Nagarajaiah KK, Fall CH, Srinivasan K. Association of birthweight and head circumference at birth to cognitive performance in 9- to 10-year-old children in South India: prospective birth cohort study. Pediatr Res. 2010, 67(4):424-9.

Vintzileos AM, Lodeiro JG, Feinstein SJ, Campbell WA, Weinbaum PJ, Nochimson DJ. Value of fetal ponderal index in predicting growth retardation. Obstet Gynecol. 1986 Apr;67(4):584-8.

Vuori E and Gissler M. Newborns 2010. Statistical report 42/2011, National Institute for Health and Welfare, Helsinki, 51p.

Wahabi HA, Alzeidan RA, Fayed AA, Mandil A, Al-Shaikh G, Esmaeil SA. Effects of secondhand smoke on the birth weight of term infants and the demographic profile of Saudi exposed women. BMC Public Health. 2013, 13:341. doi: 10.1186/1471-2458-13-341.

Walraven GE, Mkanje RJ, van Roosmalen J, van Dongen PW, Dolmans WM. Chest circumference as a screening method for low birth weight in newborns in rural Tanzania. Trop Geogr Med. 1994; 46(1):14-6.

Walther FJ, Ramaekers LH. The ponderal index as a measure of the nutritional status at birth and its relation to some aspects of neonatal morbidity. J Perinat Med. 1982, 10(1):42-7.

Wang X, Zuckerman B, Pearson C, Kaufman G, Chen C, Wang G, Niu T, Wise PH, Bauchner H, Xu X. Maternal cigarette smoking, metabolic gene polymorphism, and infant birth weight. JAMA. 2002, 287(2):195-202.

Weightman AL, Morgan HE, Shepherd MA, Kitcher H, Roberts C, Dunstan FD. Social inequality and infant health in the UK: systematic review and meta-analyses. BMJ Open. 2012, 2(3). pii: e000964. doi: 10.1136/bmjopen-2012-000964.

Weissmann-Brenner A, Simchen MJ, Zilberberg E, Kalter A, Weisz B, Achiron R, Dulitzky M. Maternal and neonatal outcomes of large for gestational age pregnancies. Acta Obstet Gynecol Scand. 2012, 91(7):844-9.

Wells JCK. What Was Human Birth Weight in the Past? Simulations Based on Data on Stature from the Palaeolithic to the Present. J Life Sci. 2009, 1(2): 115-120.

Wennergren M. Antenatal screening and risk factors for intrauterine growth retardation. Int J Technol Assess Health Care. 1992, 8 (Suppl 1): 147–151.

Werner B, Bodin L. Head circumference from birth to age 48 months for infants in Sweden. Acta Paediatr. 2006, 95(12):1601-7.

Wilcox A. On the importance—and the unimportance—of birthweight. Int J Epidemiol 2001;30:1233–41.

Wilcox AJ, Skjaerven R, Buekens P, Kiely J. Birthweight and perinatal mortality—A comparison of the United States and Norway. JAMA. 1995, 273**:**709–11.

Williams MC, Gore D and O’Brien WF. Decreased birth weight/placenta ratio and asymmetric growth restriction. Obstetrics & Gynecology. 2000, 95(4); S76–S77

Williams MC, O'Brien WF. A comparison of birth weight and weight/length ratio for gestation as correlates of perinatal morbidity. J Perinatol. 1997, 17(5):346-50.

Witter FR, Luke B. The effect of maternal height on birth weight and birth length. Early Hum Dev. 1991, 25(3):181-6.

World Health Organization (WHO). ICD-10 Version:2010. http://apps.who.int/classifications/icd10/browse/2010/en, viewed 2.9.2014.

Yaghootkar H, Freathy RM. Genetic origins of low birth weight. Curr Opin Clin Nutr Metab Care. 2012, 15(3):258-64.

Yehuda M. File, Weight vs. gestational age. Wikipedia, http://en.wikipedia.org/wiki/File:Weight_vs_gestational_Age.jpg, viewed 3.6.2013.