Early childhood head circumference:

Reference ranges for Ethiopian population

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This thesis is submitted in partial fulfilment of the requirements for the degree of Master of Philosophy in International Health at the University of Bergen.

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Summary

Background: Hydrocephalus is a condition of increased volume of cerebrospinal fluid commonly associated with impaired brain function. It is more common in developing countries and mostly frequently in children. One can expect 3000-6000 new cases of hydrocephalus annually in Ethiopia. Head circumference (HC) is commonly increased in these children and its measurement is a simple, quick and inexpensive method of screening for hydrocephalus. Early treatment, which is now available in Ethiopia, prevents or reduces the development of malfunction. Since early treatment now has become available in Ethiopia, we were motivated to establish such a method in the country.

Aims of the study: The aim of this study is to develop reference ranges for HC in Ethiopian infants and compare this reference with the existing WHO standard.

Materials and methods: This was a prospective cross-sectional study approved by the ethics review board. Children age 0-24 months attending the mother-and-child clinic primarily for vaccination program in Addis Ababa and four other main cities of Ethiopia, were recruited to the study after informed consent. Hydrocephalus or having been treated for hydrocephalus and other obvious diseases including malnutrition were not included, nor were infants without documented date of birth. A soft measurement tape was used to measure the circumference in cm in a standardized way. In addition to measuring HC age, date of birth, ethnicity, medical history were recorded for all participants. The LMS method was used to establish the reference graphs for boys and girls. These graphs were compared with WHO and Norwegian charts both by calculating absolute differences and comparing percentile lines using 95%CI.

Results: 4025 children (2046 boys and 1979 girls) under 24 months were included in the study. The established reference ranges for boys and girls had a similar pattern to those found in the WHO and Norwegian studies. The 50th and 97th percentiles of the WHO charts were found to be significantly below the corresponding Ethiopian lines. The 3rd and 50th Norwegian percentiles were significantly above the corresponding Ethiopian lines.

Conclusion: Ethiopian reference ranges for children 0-24 months of age were found to be significantly different from those established by WHO, suggesting the use of local reference for the screening for hydrocephalus. We speculate that a trend towards lower 3-percentile values with advancing age in the Ethiopian children may be due to nutritional or environmental reasons.

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List of abbreviations

AAU Addis Ababa University

BMI Body Mass Index

CNS Central Nervous System

CI Confidence Interval

CSF Cerebro Spinal Fluid

EDF Equivalent Degrees of Freedom

HC Head Circumference

HIV Human Immunodeficiency Virus

ICP Intra Cranial Pressure

LMS box-cox power Median Coefficient of variation

MGRS Multi- center Growth Reference Study

NPH Normal Pressure Hydrocephalus

RTEM Relative Technical Error of Measurement

SD Standard Deviation

TEM Technical Error of Measurement

UIB Univercity of Bergen

WHO World Health Organization

Acknowledgement

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Dedication

This dissertation is dedicated to Professor of Emeritus Knut Wester. My academic journey would have remained a dream had it not been supported by him. I cannot find words to express my heartfelt gratitude to Professor Knut who inspired me in all my academic and personal growth**.**

1. Introduction

Definition

Hydrocephalus is a congenital or acquired condition, in which there is a mismatch between production and elimination of cerebrospinal fluid (CSF), resulting in an accumulation of CSF and an increased intracranial pressure (ICP), which inevitably will cause permanent brain damage in the affected children (1-5). The human skull is filled with three compartments; brain, CSF and blood. An expansion of one compartment is at the expense of another and may result in severe and irreversible damage (6). If not treated early, it may cause brain damage with developmental delay, blindness, other neurological problems and in some cases, finally death (7).

Signs and symptoms of hydrocephalus

The signs and symptoms of hydrocephalus are mostly as a result of the increase in intracranial pressure (ICP), but infants and older children/adults with the disease may have different manifestations. As the cranial suture is not yet closed in infants, syndrome such as increased head circumference, tense fontanels, separation of the cranial suture, episodic apnea, bradycardia, and irritability may occur (8). Older children and adults' symptoms are usually non specific and reflect raised intracranial pressure, they include: headache, vomiting, altered level of consciousness, visual obscuration, papilloedema, cognitive impairment, poor concentration, and gait disturbance. The rate of onset of the symptoms varies according to the cause of the hydrocephalus (8).

Incidence and prevalence of hydrocephalus

There have been different studies done on the incidence and prevalence of hydrocephalus, but almost all are in developed countries. In these countries, pediatric hydrocephalus is mostly a congenital/developmental disorder with a rather low prevalence and incidence. The incidence of congenital hydrocephalus has been estimated to be about 0.5 cases per 1000 live births with overall incidence, including congenital and acquired forms, 3-5 cases per 1000 live births (9, 10). A study in Norway by Zahl and Wester showed an overall prevalence of hydrocephalus to be

0.75 cases per 1000 live births (1), and another recent Norwegian study found the prevalence of idiopathic normal pressure hydrocephalus (NPH) to be 21.9 per 100 000 and the incidence to be 5.5 per 100 000 (11). In Sweden, an overall prevalence of 0.82 per 1000 live births was found, and the prevalence of infantile hydrocephalus to be 0.49 and 0.33 for children with myelomeningocoele per 1000 live births (12). Another Swedish study found the prevalence of infantile hydrocephalus was 6.99 per 1000 in the 1970s (13). Analyzed data from the Czech National registry from 1961 to 2000 retrospectively found the mean incidence of congenital hydrocephalus diagnosed both pre and postnatal to be 6.35 per 10 000 live born infants (14). Similar figures can be found in other western countries. Others show that hydrocephalus is one of the most commonly encountered conditions in neurosurgery, with estimated prevalence of 1.5-5 per 10 000 live births (15).

If these prevalences and incidences of hydrocephalus from the countries mentioned above, should be applied in the developing world, these estimates are likely too low. Moreover, children born with hydrocephalus in Europe, United States, Japan, and other western societies are likely to receive surgical attention in the immediate perinatal period or as soon as possible in order to prevent cerebral damage from increased intracranial pressure.

Hydrocephalus is also a disease of poverty causing a considerable burden in developing societies such as in Sub-Saharan Africa. The incidence in this region is not yet known, but believed to be higher than in developed countries. According to a conservative estimate by Mubashir Mahmood et al., only in East, Central, and Southern Africa region – an area with a combined population of more than quarter billion (250 million) – the annual incidence of hydrocephalus in infants is suggested to exceed 14 000 new cases (16). Ben Warf has studied hydrocephalus in Uganda, and he estimates that the incidence is much higher than in high-income countries. Based on his estimates, 1000-2000 children with hydrocephalus are born each year in Uganda, a country with a population of 28 million. Warf points out that this high incidence most likely is caused by infections, probably 60% of the cases. Central nervous system (CNS) infection such as meningitis and ventriculitis during the first months of life, are the most common causes. In this study, 265 (57%) out of 468 hydrocephalus patients were post infectious, 136 cases (29%) were non-post infectious. Hydrocephalus associated with myelomeningocele was seen in 61 cases (13%) and associated with encephalocele in five cases (1%). In one patient, the hydrocephalus was the probable result of a neonatal intraventricular hemorrhage. The study also tries to investigate whether there is a correlation between hydrocephalus and HIV, but failed to find an association. However, the open neural tube defect may in some hydrocephalus patients increase the likelihood of mother to child transmission of HIV (17). Placing cow dung on the umbilical stump, which is a harmful traditional practice common in Ethiopian rural areas, may also contribute to infection (18). HIV and malnutrition, which are quite common in sub-Saharan East African countries, are known to predispose people to infection. There is therefore reason to believe that malnutrition and consequent infections also play an important role in the etiology of hydrocephalus. The Ethiopian incidence is more likely to be closer to that of Uganda than in European or North American countries. Based on the above estimate of Warf for Uganda, we can also anticipate the Ethiopian incidence. The population of Ethiopia is approximately three times that of Uganda. Provided that the Ethiopian incidence of hydrocephalus is equal to that of Uganda, one can expect 3000-6000 new cases of hydrocephalus annually in Ethiopia. Only a small fraction of these children will be detected early enough to prevent brain damage, and most will probably survive with severe neurological and mental deficits, thus, creating a burden to society and their families. We have made preliminary observations in Addis Ababa indicating that the prevalence there is 6 - 8 times higher than in the western world.

On top of the high incidence and prevalence in Africa, hydrocephalus comes the challenge of lacking trained neurosurgical personnel, inadequately equipped public health care facilities, scant resource allocation, high rates of neonatal infections, poor infrastructure, difficulty in reaching specialized hospitals that are able to treat hydrocephalus, and high complication rates in patients who are able to access and receive shunting procedures (16). To conclude, it is a reason to believe that the prevalence of hydrocephalus in Africa is many times higher than that of developed nations, and that most cases have an infectious etiology.

Neurosurgery and hydrocephalus in Africa

According to Kalangu's study on pediatric neurosurgery in Africa in 2000, the problem of hydrocephalus is complex because most people, including hydrocephalus patients, live in rural areas far from medical expertise (7). Therefore, most relatives of hydrocephalic children will not be aware of the possibility of effective treatment, and if they were, they would likely not be able to afford to travel to medical centres where such treatment is available. In Ethiopia, this sort of treatment is currently available only in Addis Ababa. Even those who get diagnosed will be delayed during their referral process by lack of awareness of treatment options or by seeking help from traditional healers. On top of this, there is a scarcity of neurosurgeons. There are 565 neurosurgeons on the African continent, making a ratio of 1 neurosurgeon per 1 352 000 people, whereas the ratio was 1 per 230 000 people in the whole world. In developed countries that ratio can be even 1 per 81 000 people. The difference in ratio of neurosurgeons per population is substantial even within Africa. Countries such as Egypt (with 165 neurosurgeons), Algeria (130) and other North African countries are on one extreme side with a ratio of 1 per 400 000; whereas sub-Saharan countries such as Ethiopia have only a fraction of that (7).

A study in Kenya showed that among 2000 children with hydrocephalus who were born over the course of a year, only a lucky 1/4th (500-600 children) will undergo the surgical shunting procedure. The rest, 3/4th of the cases, remain unfortunate, and do not get a chance of receiving treatment at all (19).

In Africa where health-seeking behaviour is low, the birth of a child with hydrocephalus can be taken as a personal failure because certain traditions and cultures think it represents annoyance from gods or ancestors. Studies from Nigeria in 1985 and in Cameroon in 2011 mention that "many parents have tried to hide their children's condition from friends, neighbours, and extended family, so pressure was exerted on mothers by their families to get rid of the hydrocephalus child by abandonment in the bush" (20, 21). Thirty-two years later, in 2014, African children and their desperately helpless parents, still face immense difficulties.

Neurosurgeons in Ethiopia

Hydrocephalus remains a neglected and undertreated pediatric neurosurgical problem in Ethiopia. Only four neurosurgeons were practicing in Ethiopia in 2006, caring for more than 70 million residents, giving a ratio of 1 neurosurgeon per 17.5 million inhabitants. In the future, this situation will change, as a training program in neurosurgery has been running since 2006, with 6 more neurosurgeons already graduating, and 20 more residents currently being trained. Thus, along with the building-up of the neurosurgical expertise, it is important to improve the diagnostic tools for detecting hydrocephalus at an early stage.

Head circumference measurement as a screening tool for hydrocephalus

The most commonly used anthropometric measurements for the assessment of growth in child clinics are length/height, weight and head circumference (HC) or occipito-frontal circumference (8) reflecting general health and nutritional status of infants. HC can help us monitor the growth of the brain, because cognitive function, intracranial volume, and brain volume are closely related to the magnitude of HC (22, 23). Measuring HC is essential when doing physical examinations, particularly when screening for disorders associated with macrocephaly or microcephaly. The measurement of HC is an easy, non-invasive, and inexpensive method routinely included in the physical examination of infants and children. In infants, rapid increase in head size suggests the presence of hydrocephalus, while microcephalus can be associated with structural brain abnormalities or genetic syndromes (24). In adults, the diagnosis of hydrocephalus associated with macrocephaly suggests that the cause of this process occurred before the complete closure of sutures and fontanels (25), while microcephalus may reflect a pathogenic mechanism such as idiopathic intracranial hypertension (26).

Therefore, routine measurement of HC in children is a diagnostic tool of utmost importance to achieve early detection and treatment, hopefully before permanent brain damage has occurred. In infants and small children, the CSF accumulation and enhanced intracranial pressure causes the skull to expand, and the condition can therefore be detected by a HC that grows too rapidly. In western countries, pediatric hydrocephalus is most commonly discovered at an early stage by such routine HC measurements as Zahl and Wester showed in their nation-wide study from Norway; 173 (58%) out of 298 neurosurgical pediatric patients were diagnosed with hydrocephalus, 57 patients (19%) had an intracranial tumor and the rest 68 (23%) had several other intracranial conditions. Out of all cases, 138 (46%) were diagnosed because of an increased HC, which was the only symptom in 109 (79%) patients. Seventy-six percent of the hydrocephalic children were diagnosed before 12 months of age (1). Early and routinely measuring of HC is also important in diagnosis of brain cancer (17).

Because of the rapid growth of the brain compared with the rest of the body, the head circumference increases correspondingly faster than height and weight in the early years. Thus, at any given age, the brain is closer to its adult size than are height and weight. By the age of nine months, the brain has reached half of its adult size, and at the age of two years, the brain and therefore the HC, has reached nearly 80% of the adult size, whereas height and weight have reached only 50%. Due to this rapid early growth of the brain, the head circumference is more liable to be affected by malnutrition or diseases in the early years (10).

In early infancy the skull bones are not fused, which allows for brain growth. The rate of increase in HC differs for different ages. During the first three months it is 3 cm per month, and then the anterior fontanel closes between 9-18 months. For children between 4 and 6 years of age, HC growth is only one cm per year (6).

The cut-off for defining small or large heads varies in the litterature. Macrocephaly (an abnormally large head) in the United States is defined as a head circumference above the 95th percentile (for normally distributed HC values corresponding to 1.64 standard deviations from the mean of gender and age specific controls) (27). WHO recommends using the more extreme 97th percentile (28), and the 98th or 99.6th percentiles are proposed in the United Kingdom (29). A national guideline of Norway used the 3rd and the 97th percentiles specifying that a child whose HC has crossed two major percentile lines should be referred for further evaluation (1).

Various studies show that serial measurements of the head circumference are more important than a single measurement. It is known from other studies that the timing for completion of suture closure depends on the site of the suture, sex of the child and ethnic background (6). In 2006 WHO prepared a multi-centre growth reference study (MGRS), based on data from six countries (Brazil, Ghana, India, Norway, Oman, USA). All sites included children who were from affluent societies and who were well-nourished based on the recommendation of WHO MGRS. The ambition was to create a «standard», showing how children in any part of the world «should grow» (28). Because of variation in growth between different populations, many countries have prepared their own growth standards.

Juliusson et al. found fewer children below -2SD and more children above +2SD when comparing Norwegian and Belgian data with the WHO standard. This was true for length/height, weight, BMI and HC. The largest discrepancy was found for HC with the overall percentage below -2SD being 0.97% (0.70-1.33) for Belgian and only 0.18% (0.05-0.53) for Norwegian children. The prevalence of children above +2SD was relatively high in both countries; in Belgium it was 6.55% (5.76-7.42) and in Norway 6.40% (5.19-7.83). In addition, they found the largest discrepancy in the age group from 1 to 3 years. They also observed that the growth of children in both Belgium and Norway was generally closer to that of the local reference population than to that of the WHO standard. Based on this, they recommended use of their local growth references for monitoring growth of children rather than using the WHO growth standards (30).

Significance of the present study

Ethiopia is among the African countries that are highly affected by malnutrition causing stunting, i.e. restricted height (50.7%) and underweight (34.6%) of children less than five years of age(31). On top of this, pediatric hydrocephalus is among the neglected diseases that have severe health, social and economic impact on the affected families and communities. As mentioned, it can be detected by the simple routine of HC measurement(1).

Taking into account facts such as expected high prevalence and incidence of hydrocephalus, extreme shortage of expertise in neurosurgery and to the lack of a national screening reference, a first step to improve the care for hydrocephalus in Ethiopia would be to establish reference ranges and screening routines. Six years ago, the universities of Addis Ababa and Bergen began a collaborative training of neurosurgeons. As a consequence of this, the accessibility for hydrocephalus treatment has improved. Therefore, the present study aims at establishing reference ranges for HC in Ethiopia.

2. Objectives of the study

Main objective

To develop reference ranges for head circumference (HC) for Ethiopian infants

Secondary objectives

1. To compare these new reference ranges for head circumference with the existing WHO standard.

2. To compare the new reference ranges for head circumference with a Norwegian standard

3. Research design and method

General design type

The study design was a prospective, observational cross-sectional study. HC was collected in healthy children who full fill the inclusion criteria and visited the mother and child clinics at three health centers in Addis Ababa and four health centers in the cities Mekele, Dessie, Dire Dawa and Nazeret.

Study area and target population

According to a WHO report for world health statistics in 2012, the total population of Ethiopia was estimated to be 82 950 000 and those younger than 15 years to constitute 41% of the population. The annual population growth rate of Ethiopia is 2.3%, which is close to the African regional growth rate (2.4%). The total fertility rate (4.2%) is less than for the African average (4.8%). Neonatal, infant and under five year mortality per 1000 live births in Ethiopia is 35, 68 and 106, respectively, while the African average is 34, 75 and, 119 in the same order (32).

Administratively, Ethiopia is structured into nine regional states: Tigray, Affar, Amhara, Oromiya, Somali, Benishangul-Gumuz, Southern Nations Nationalities and Peoples (SNNP), Gambela, and Harari in addition to two city administrations, that is, Addis Ababa and Dire Dawa Administration Councils. The country is home to more than 80 ethnic groups, which vary in population size from more than 26 million to fewer than 100. The ethnic composition of the country is shown in the Annex 1. The largest ethnic groups are Oromo (34.5%), Amhara (26.9%), Somali (6.2%), Tigray (6.1%) and Gurage (2.5%)(32).

Addis Ababa, located about 2,400m above sea level at 9.02° N 38.44° E, is the capital city of Ethiopia. According to the census conducted in 2007, the population of Addis Ababa is 2 739 551, of whom 1 305 387 are men and 1 434 164 women. It is estimated that presently there are no rural parts of the city. As it is a capital city, all Ethiopian ethnic groups are represented in the following pattern: Amhara (47.04%), Oromo (19.51%), Gurage (16.34%), Tigray (6.18%), Silt'e (2.94%), and Gamo (1.68%) and others (6.31%)(33). The city is administratively divided into 10 parts. There were 26 health centers at the beginning of the data collection, these have now increased to about 56; all health centers provide maternal and child health services. These health clinics are non-profit units rendering services to the public.

Source Population: all children aged ≤24 months who visit the maternal and child health clinic for any reason.

Study Subjects/Child population: a total of 4025 children who fulfil the inclusion criteria were measured and included in the study. The data were collected over approximately four years; from October 2009 to July 2013. This cross sectional study includes measurements from 2046 boys and 1979 girls. All the children had both a father and a mother who are Ethiopians. Only two children originated from foreign countries (Eritrea and Yemen) that are also excluded from analysis.

We had formal approval collect data from all the 24 health clinics in Addis Ababa and any health center in the country. However, the project had limited manpower. After having visited most of the city's clinics, the project focused on three large health centers in Addis Ababa and four other health centers outside the city to maximize data collection within the allotted research period. The clinics were arbitrarily selected, but priority was given to those with high numbers of children and within reasonable distance to make the daily work efficient. The health centers cared for both adults and children. They had department including family planning, a small maternity ward, a vaccination office, and an out-patient treatment centre for both children and adults. We measured all children who came for their vaccinations. The immunization department had high turnover rates on Monday, Thursday and Friday because vaccination campaigns were offered on those days. Children between 0 - 24 months of age were not a part of a national follow-up program for children, and therefore not routinely asked to come to the health clinics for anthropometric. They visited the health clinics for one of the three following purposes: 1) to participate in the vaccination programme, 2) to participate in a follow-up programme concerning nutrition and HIV-prophylaxis, or 3) because they had various medical problems.

Inclusion Criteria: all children who came to the health center, maternal and child clinic for routine immunization service, and who were ≤24 months of age.

Exclusion Criteria: any child with a suspected or diagnosed intracranial expansive condition, having been born with congenital problems of the head, a history of chronic illness, visible malnutrition problems, and/or a child with either of the parents who did not belong to any ethnic group in Ethiopia were excluded from the study. Signs and symptoms of hydrocephalus were obvious expansion of head, neurological signs and deficits and distended veins of the scalp. Previous treatment of intracranial lesions

Data Collection procedures

Measurement technique. After getting the permission of the medical director and the head of maternal and child care at the health center, we explained the overall aim, procedure and the importance of measuring the HC of the baby. Soon we got the consent of the parents or caregivers, we measure HC of the baby three times and taking the average record.

A total of three study workers, the principal investigator and two co-investigators, measured all children in the study. Three Norwegian medical students (Mari Idsøe, Miriam Wiksnes, Thomas Moss) measured approximately 1000 children, and the principal investigator (EB), measured 3025 children. A standardized technique was used measuring the maximal occiputo frontal circumference (HC). After parents or caregivers agreed to participate in the study, they were asked to remove any of the child's hair ornaments or braids. Children were placed on parents/caregivers lap to feel safe and comfortable, and a head circumference tape was placed around the child's head so that the tape was situated across the frontal bones of the skull; immediately above the eyebrows; perpendicular to the long axis of the face; above the ears and over the occipital prominence on the back of the head. The tape moved up and down over the back of the head in order to always locate the maximal circumference. The tape measure was made to be neither too loose nor too tight, so that it fit comfortably around the head, but also compressed the hair and underlying soft tissues. The measurement was read from lateral side. The HC was measured to the nearest 0.1 cm. Since the HC tape shows both centimetres and inches, checking that the metric scale is used was very important. Finally, the HC tape was removed and the enumerator proceeded to the next measure(34). In addition to HC measuring, it was necessary to have a small interview with parent or caregiver who accompanied the child to the clinic

Ethiopia uses a different calendar than western countries, which is based on the old Coptic calendar (35). The calendar year has 13 months, and is between seven and eight years behind the Gregorian calendar, also known as the Western calendar. Children's date of birth was given to us on the Ethiopian calendar.

Pilot study: a small pilot study was first performed, showing that the collection of data, including HC measurements, should be done by well-trained personnel. And this is shown by when the measuring was conducted by untrained personnel without supervision they always tended to round off the HC measurements to the closest whole cm, without any decimals. The pilot study also revealed that a lot of information around the children's health was not recorded when these personnel measures HC. So we have found that was important to collect the data by a trained person whose precision is to the standard.

Recording the results

The following information was collected: sex, age, date of birth, date of measurement, ethnicity of the father, ethnicity of the mother, ethnicity of the child (if mixed; taking paternal ethnicity which is customary in Ethiopia) and HC in cm and mm. More than three-quarters of the data were directly entered into the data base using Ipad, and the rest 1/4th on a prepared worksheet.

The child age, calculated by subtracting the date of birth from date of measurement, was cross-checked with age given by the parents/care providers. For consistency, we asked date of birth from the parents/caregivers and cross-checked with what was registered on the immunization card.

Data management and analysis

The collected data were organized in Excel. Measurements below – 4 SD or about + 4 SD were defined as outliers, and removed. Thirteen measurements for boys and nine for girls were removed leaving us with 4019 data for the final analysis.

Statistics and calculations:

Reference curves for head circumference were estimated with the LMS method by Cole and Green(36). The LMS method is a semi-parametric method that uses the box-cox power transformation to normalize the distribution of the parameter of interest (i.e. head circumference) conditional on age. Smooth curves for the box-cox power (L), median (M), and coefficient of variation (S) are estimated over the whole age-range with cubic splines by maximizing the penalized likelihood. The degree of smoothing is controlled by assigning a number of equivalent degrees of freedom (edf) for each curve. Two edf will result in a straight line, and three or more edf allow for more variation by age. With one edf the corresponding parameter (L, M or S) is constant (the same at all ages), and the edf are zero when a fixed value is used.

Models are initially selected by a deviance criterion, and goodness of fit is assessed using several tests for normality of the model residuals. With the LMS coefficients, smooth percentile curves can be calculated from $C = M*(1 + S*z_\alpha)^{(1/L)}$ when $L \neq 0$, and $C = M*\exp(S*z_\alpha)$ when $L = 0$; where z_α is the quantile of the standard normal distribution that corresponds to the percentile $100*\alpha$. Measurements are converted to standard deviation scores (SDS) or z-scores from $z = [(y/M)^L – 1]/[L*S]$ when $L \neq 0$, and $z = \log(y/M)/S$ when $L = 0$; where y is a measurement at age t, and L, M, and S are the corresponding parameters at that age. Standard errors and confidence intervals for percentiles were estimated from 500 bootstrap samples. The charts were drawn with the help of Microsoft Excel 2007 (37).

Quality control

Equipment: A non-stretchable measurement tape was used and checked for variation when used repeatedly, getting wet or getting warm. To check for these we tested our measurement tape against a fixed standard (metal) when we started to use it, and again after using it for a period of time.

Observer reliability assessment: before initiation of the data collection, the principal investigator trained anthropometric measurement techniches for five days at Haukeland University Hospital, Bergen. Then he participated in a test and re-test exercise for head circumference at CIH. These were anthropometric measurements of 10 Norwegian children. Measurements were performed twice, with an interval of at least 15 minutes. He compared his measurement technique with that of the supervisor (Petur Juliusson), acting as the reference standard.

Selection bias study: to avoid the likelihood of selection bias, data collectors stayed in the health centers and measured all children who came in during the working hours and fulfilled the inclusion criteria, from 8:30AM to 12:00AM.

Sampling procedures: health centers were selected arbitrary according to the criterion of having high under two patient clients. Then, any children coming to these health facilities for normal routine service, and that fulfilled the inclusion criteria were measured.

Sample size determination

Because of rapid growth during the first two years of life, more measurements are needed than later in childhood. Generally, 200 girls and 200 boys are thought of as sufficient for each age group above two years of age. This number has been suggested to be doubled between 1-2 years of age, and increased by factor 4 in the first year of life. Therefore, based on the experience from a previously published study, we aimed at including 1600 children ≤1 year of age and 800 children 1-2 years of age (38).

Ethical considerations

The study is an extension of a project approved by the Regional Committee for Medical and Health Research Ethics, Norway (REK in 2006) aiming at training Ethiopian neurosurgeons in a collaboration between Addis Ababa University and University of Bergen. The study is also approved by the Addis Ababa University institutional review board (MFGC/058/07) (Annex1). The participants' parent/caregiver gave oral consent. The consent form explained the purpose of the study (Annex 2). The recorded data were stored on a laptop secured with a password and kept locked up when not in use. Data analysis and reporting were carried out with de-identified datasets.

4. Result

We included participants from 3 clinics of a total 26 existing in the Addis Ababa and four other cities (Mekele, Dessie, Nazeret and Dire Dawa). Of the estimated 115 200 children yearly attending the clinics, 50 000 would be in the age group 0-24 months. The flow chart in figure 1 gives the overview of the participants. Table 1 and 2 showes the age distribution for both sexes. The participation rate was almost 100% in all health centers. There were only two refusals, both claiming that not important to participate in the study.

Measurements of totally 4025 children were used to established reference charts for the HC for girls and boys (table 1 and 2) and corresponding graphs with 3rd, 50th and 97th percentil (figure 2 and 3). Using the LMS method by Cole and Green(36), the curves were modeled without skewness, with the L fixed as 1, edf=0. The edf for the M curve were 6 and for the S curve 3 for the boys and the corresponding figures for the girls were 5 and 4. The age was rescaled.

Based on the data from this measurement session, the technical error of measurement (TEM) was 0.191 and the relative TEM 0.39%, and for the supervisor the numbers were 0.176 0.36% reflecting good precision (expert TEM is supposed to be below 0.15) (34).

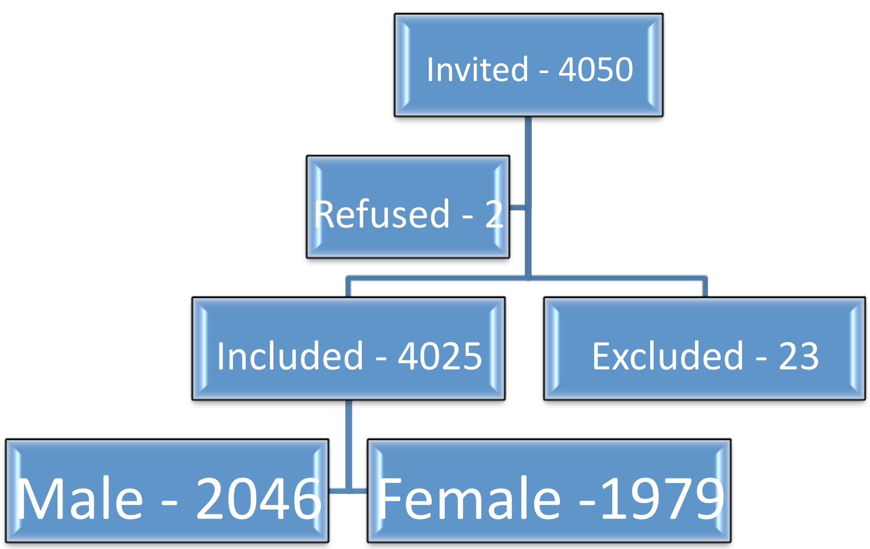


Figure 1, Flow chart showing the distribution of participants in the study.

Table 2 Head circumference(in cm) and box-cox power, median, and coefficient of variation value for girls from 0-24months of age in Ethiopian population.

Age(month)	n	l	m	s	3rd p	10th p	25th p	50th p	75th p	90th p	97th p	-2SD	0	+2SD
0	195	1	34.78476	0.040785	32.11646	32.96661	33.82786	34.78476	35.74167	36.60291	37.45307	31.94734	34.78476	37.62218
1	301	1	36.91077	0.037228	34.32634	35.14977	35.98394	36.91077	37.8376	38.67178	39.49521	34.16253	36.91077	39.65901
2	242	1	38.65311	0.03526	36.08973	36.90645	37.73383	38.65311	39.57239	40.39977	41.21649	35.92726	38.65311	41.37896
3	233	1	39.97524	0.034829	37.35658	38.19091	39.03614	39.97524	40.91434	41.75956	42.59389	37.19061	39.97524	42.75987
4	95	1	41.02286	0.034991	38.3231	39.18328	40.05467	41.02286	41.99104	42.86244	43.72261	38.15199	41.02286	43.89372
5	38	1	41.8988	0.035109	39.13212	40.01362	40.90661	41.8988	42.89098	43.78398	44.66547	38.95677	41.8988	44.84083
6	48	1	42.6273	0.035014	39.82012	40.71452	41.62059	42.6273	43.63401	44.54008	45.43448	39.6422	42.6273	45.6124
7	34	1	43.23261	0.034872	40.39711	41.30053	42.21574	43.23261	44.24948	45.16469	46.06811	40.21739	43.23261	46.24783
8	152	1	43.74373	0.034771	40.88304	41.79449	42.71783	43.74373	44.76963	45.69297	46.60442	40.70173	43.74373	46.78573
9	140	1	44.18281	0.034753	41.29487	42.215	43.14713	44.18281	45.21848	46.15062	47.07075	41.11183	44.18281	47.25379
10	33	1	44.567	0.03483	41.64751	42.57769	43.52001	44.567	45.61398	46.5563	47.48648	41.46248	44.567	47.67152
11	33	1	44.90526	0.034946	41.95383	42.89419	43.84682	44.90526	45.9637	46.91633	47.85669	41.76677	44.90526	48.04375
12	30	1	45.20219	0.035054	42.22202	43.17154	44.13344	45.20219	46.27094	47.23284	48.18236	42.03313	45.20219	48.37124
13	38	1	45.45956	0.035135	42.45555	43.41266	44.38226	45.45956	46.53686	47.50646	48.46358	42.26515	45.45956	48.65397
14	69	1	45.68427	0.035187	42.66091	43.62419	44.60003	45.68427	46.76851	47.74436	48.70763	42.46929	45.68427	48.89926
15	45	1	45.88571	0.035218	42.84637	43.81473	44.79574	45.88571	46.97567	47.95668	48.92504	42.65373	45.88571	49.11768
16	29	1	46.06836	0.035232	43.01567	43.98829	44.9736	46.06836	47.16311	48.14842	49.12105	42.82219	46.06836	49.31453
17	36	1	46.23432	0.035235	43.17039	44.1466	45.13554	46.23432	47.33311	48.32205	49.29825	42.9762	46.23432	49.49245
18	34	1	46.3831	0.035231	43.30967	44.2889	45.28091	46.3831	47.48529	48.4773	49.45653	43.11488	46.3831	49.65133
19	30	1	46.51844	0.035223	43.43672	44.41859	45.41328	46.51844	47.6236	48.61828	49.60015	43.2414	46.51844	49.79548
20	41	1	46.64508	0.035213	43.55582	44.5401	45.53721	46.64508	47.75296	48.75007	49.73435	43.36002	46.64508	49.93015
21	24	1	46.76775	0.035203	43.67129	44.65785	45.6573	46.76775	47.8782	48.87764	49.86421	43.47503	46.76775	50.06046
22	28	1	46.88762	0.035192	43.78419	44.77298	45.77467	46.88762	48.00057	49.00226	49.99105	43.58749	46.88762	50.18775
23	14	1	47.0052	0.035181	43.89497	44.88592	45.88981	47.0052	48.12059	49.12448	50.11543	43.69784	47.0052	50.31256
24	17	1	47.12239	0.035169	44.0054	44.99851	46.00458	47.12239	48.2402	49.24626	50.23937	43.80785	47.12239	50.43693
Total	1979													

n-number of children, l- box-cox power, m-median, s-coefficient of variation, p-percentile, SD-standard devation

Table 1 Head circumference(in cm) and box-cox power, median, and coefficient of variation value for boys from 0-24months of age in Ethiopian population.

Age(month)	n	l	m	s	3rd p	10th p	25th p	50th p	75th p	90th p	97th p	-2SD	0	2SD
0	171	1	34.92275	0.039874	32.30373	33.13818	33.98352	34.92275	35.86198	36.70732	37.54177	32.13774	34.92275	37.70777
1	305	1	37.54167	0.037897	34.86582	35.71838	36.58206	37.54167	38.50128	39.36496	40.21752	34.69622	37.54167	40.38712
2	272	1	39.45769	0.036412	36.75552	37.61646	38.48864	39.45769	40.42674	41.29892	42.15986	36.58425	39.45769	42.33113
3	246	1	40.96765	0.035553	38.22822	39.10103	39.98523	40.96765	41.95006	42.83427	43.70708	38.05459	40.96765	43.88071
4	76	1	42.15627	0.03503	39.37882	40.26374	41.16022	42.15627	43.15231	44.04879	44.93371	39.20278	42.15627	45.10975
5	42	1	43.07472	0.034599	40.27173	41.16479	42.06951	43.07472	44.07993	44.98465	45.87771	40.09407	43.07472	46.05537
6	52	1	43.80137	0.034233	40.98118	41.87973	42.79	43.80137	44.81275	45.72302	46.62156	40.80244	43.80137	46.80031
7	43	1	44.38228	0.033945	41.54878	42.45156	43.36613	44.38228	45.39843	46.313	47.21578	41.36919	44.38228	47.39537
8	125	1	44.86092	0.033718	42.01601	42.92243	43.84068	44.86092	45.88117	46.79942	47.70584	41.83569	44.86092	47.88616
9	183	1	45.2799	0.033535	42.42398	43.33391	44.25571	45.2799	46.30409	47.22589	48.13582	42.24297	45.2799	48.31683
10	53	1	45.66005	0.033383	42.79321	43.70661	44.63194	45.66005	46.68815	47.61348	48.52689	42.6115	45.66005	48.70859
11	25	1	46.0058	0.033251	43.12872	44.04539	44.97402	46.0058	47.03758	47.96621	48.88288	42.94636	46.0058	49.06523
12	44	1	46.31949	0.03313	43.43326	44.35285	45.28443	46.31949	47.35454	48.28612	49.20571	43.25033	46.31949	49.38864
13	22	1	46.59959	0.03302	43.70561	44.62767	45.56175	46.59959	47.63743	48.57151	49.49356	43.52219	46.59959	49.67699
14	56	1	46.84417	0.032919	43.9439	44.86796	45.80407	46.84417	47.88426	48.82038	49.74444	43.76007	46.84417	49.92826
15	61	1	47.05406	0.032828	44.14882	45.07446	46.01218	47.05406	48.09594	49.03366	49.95931	43.96468	47.05406	50.14344
16	40	1	47.23857	0.032745	44.32931	45.25623	46.19525	47.23857	48.28189	49.22091	50.14784	44.14491	47.23857	50.33223
17	36	1	47.40222	0.032669	44.48966	45.41764	46.35772	47.40222	48.44673	49.38681	50.31479	44.30506	47.40222	50.49939
18	42	1	47.54121	0.032603	44.62601	45.55483	46.49576	47.54121	48.58666	49.52759	50.4564	44.44125	47.54121	50.64117
19	28	1	47.65377	0.032549	44.73653	45.666	46.60759	47.65377	48.69995	49.64154	50.57101	44.55163	47.65377	50.75591
20	39	1	47.7444	0.032505	44.82555	45.75553	46.69764	47.7444	48.79115	49.73326	50.66324	44.64055	47.7444	50.84824
21	26	1	47.82101	0.032468	44.90083	45.83123	46.77377	47.82101	48.86824	49.81079	50.74119	44.71574	47.82101	50.92627
22	20	1	47.89606	0.032431	44.97458	45.9054	46.84836	47.89606	48.94376	49.88672	50.81754	44.78942	47.89606	51.00271
23	14	1	47.97715	0.032392	45.05428	45.98554	46.92895	47.97715	49.02535	49.96876	50.90002	44.86903	47.97715	51.08527
24	25	1	48.06743	0.032348	45.14303	46.07477	47.01868	48.06743	49.11618	50.06009	50.99183	44.95767	48.06743	51.17719
Total	2046													

n-number of children, l- box-cox power, m-median, s-coefficient of variation, p-percentile, SD-standard devation

Figure 2 and 3 displays the HC reference for girls and boys, respectively:

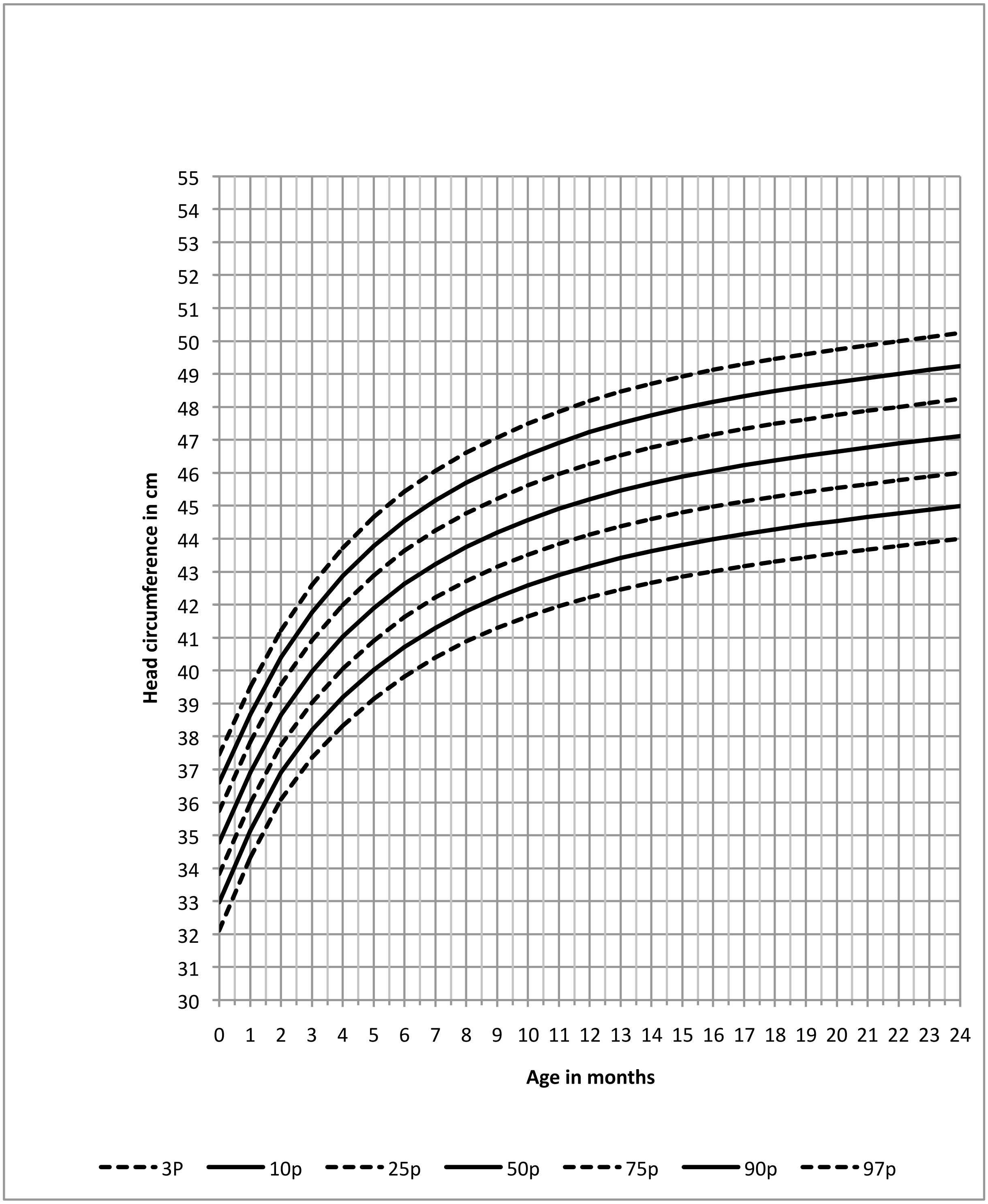


Figure 2. Ethiopian head circumference reference range for girls age 0-2 years. P=percentile

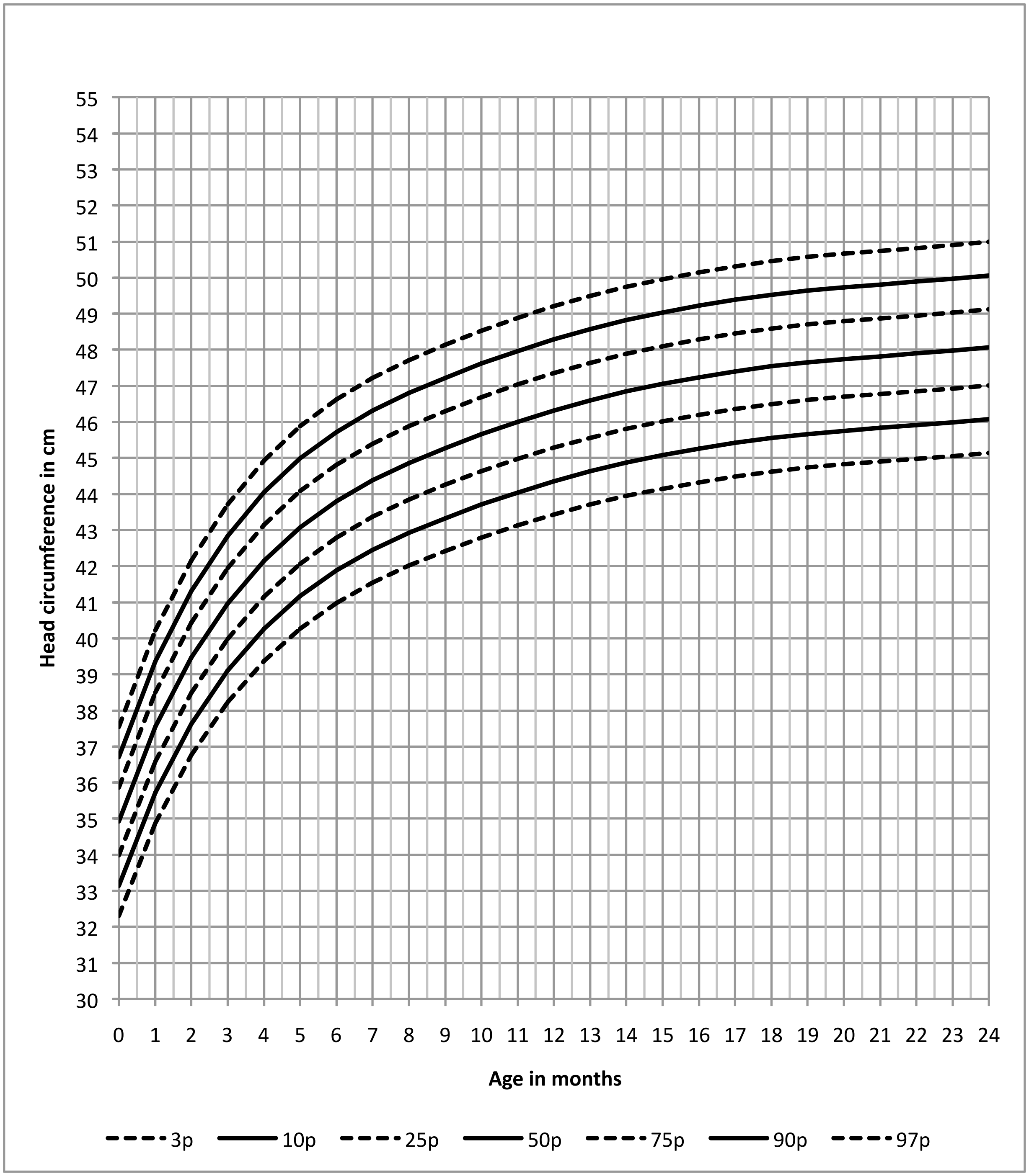


Figure 3. Ethiopian head circumference reference for boys age 0-2 years. P=percentile

Comparison of HC in between Ethiopian boys and girls aged 0-2 yrs

The HC ranges for Ethiopian boys and girls were compared using the 3, 50, and 97 percentiles (figure 4 and 5) showing a shift upwards for boys compared with girls. The difference for all percentile is almost proportional.

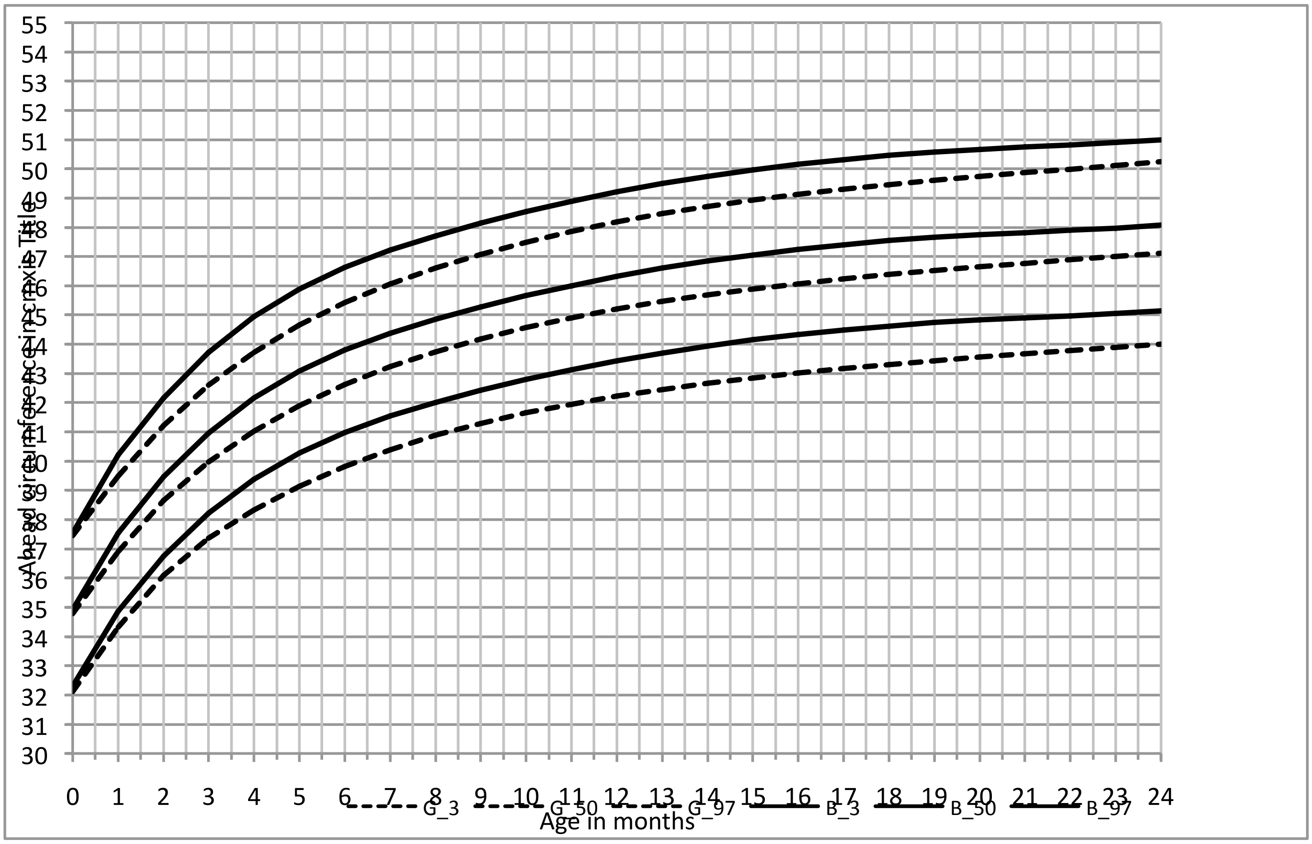


Figure 4. Comparison of reference ranges for boys (solid lines) and girls (dotted lines) for age 0-24 months in Ethiopia. P=percentile, G-girls, B, boys

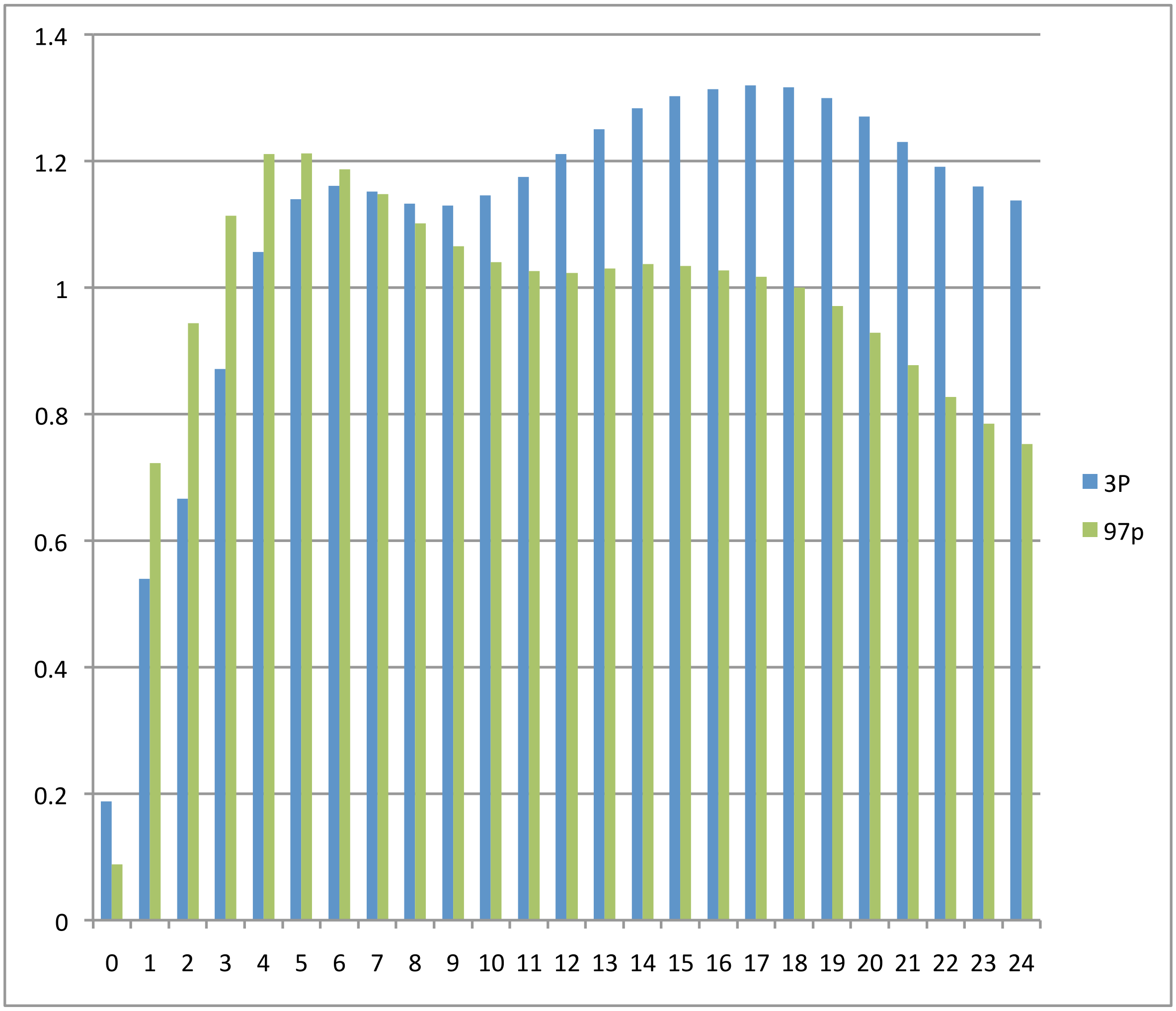
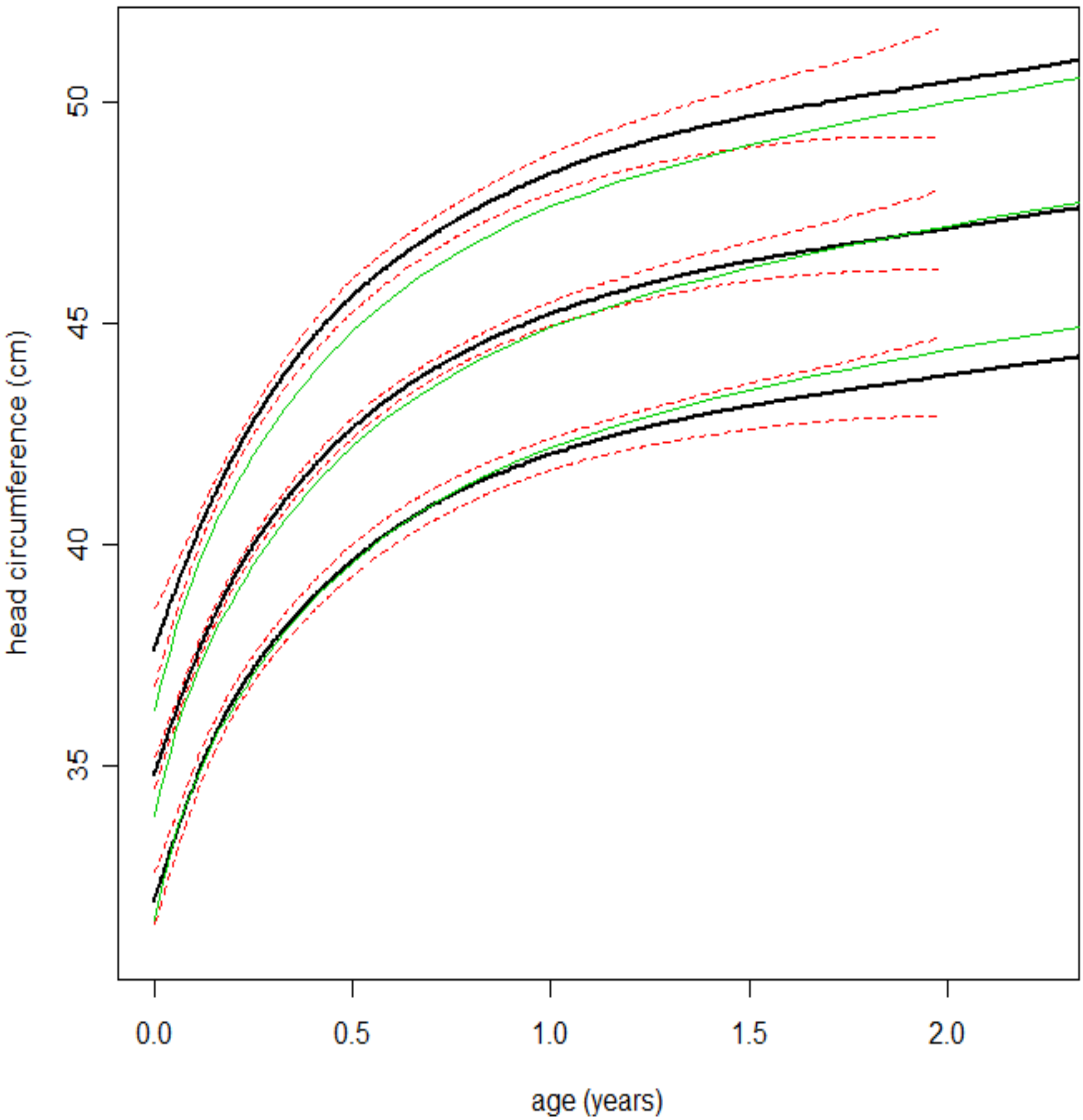


Figure 5. Difference in head circumference (cm), between the Ethiopian boys and girls for both 3- and 97-percentile. Values above zero indicate that boys have larger head circumference than girls.

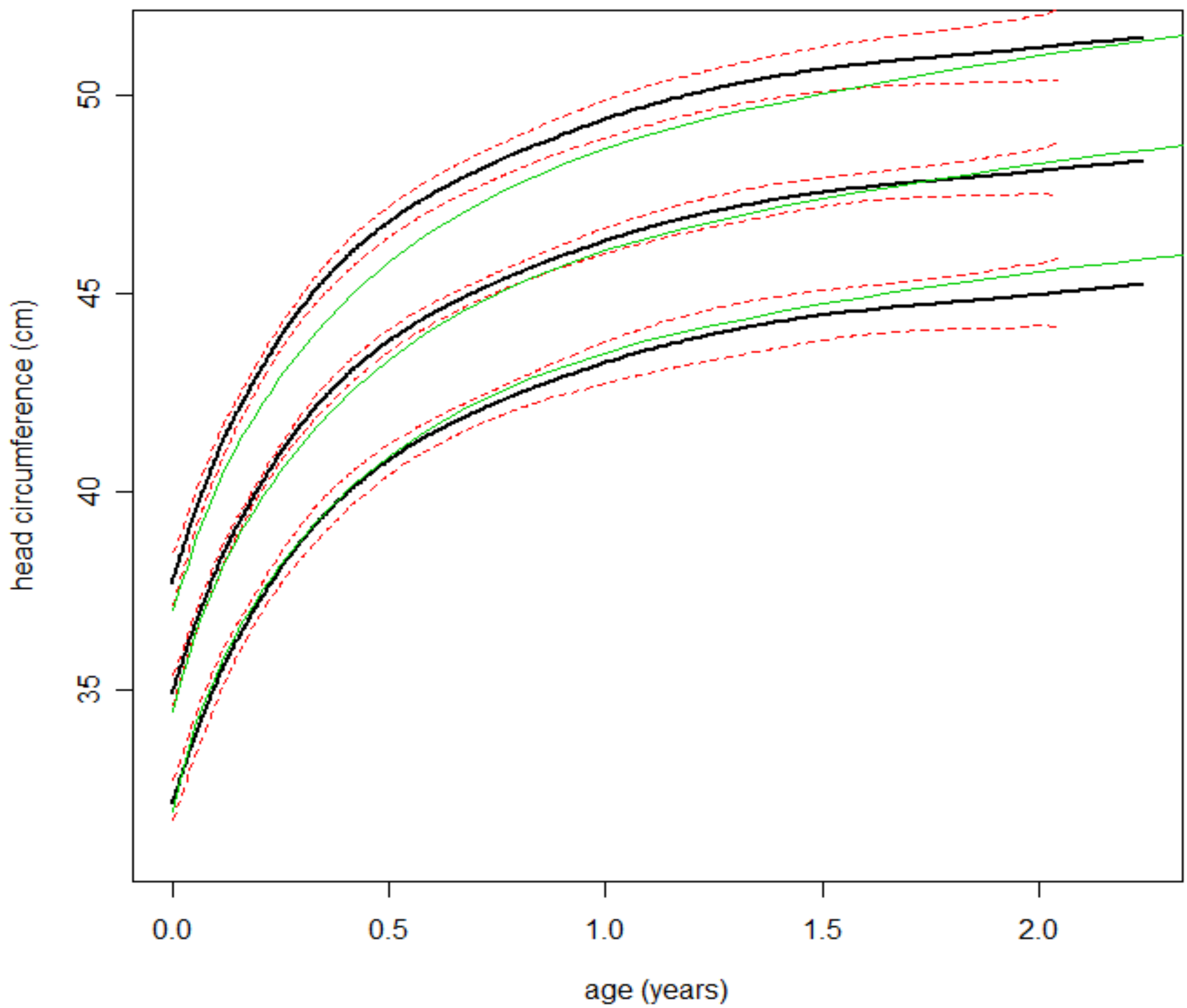
As we see from the bar graph (figure 5) for both percentiles boys are greater than girls. In both percentile the minimum difference is at birth and it is 0.19 cm for 3-percentile and 0.09 cm for 97-percentile. In the 3-percentile with increasing age the difference also increases and reaches to its maximum 1.3 cm at the age of 19 month. In the 97 percentile up to the age of 6 months with increasing age the gap is also increasing, but since then it starts to decrease. For both percentile in almost all age the difference is more or less similar, except a wide gap occurs in late age.

Comparison of Ethiopian curves with the WHO curves.

The HC growth charts for Ethiopia and WHO (39) in both girls and boys were compared using the 3, 50, and 97 percentiles (Figure 6). We used the 95%CI for the 3-, 50-, and 97-percentile for our reference ranges but did not have the access to the corresponding values for the WHO study when assign visually the difference. For both girl and boys the 3- and 50-percentile of the WHO study is encompassed by the 95%CI of our study and therefore statistically not different. For the 97-centile that is not the case for all ages but the distance is small and the comparison incomplete since the absence of the 95%CI of the WHO lines prevents assessing whether the confidence intervals overlap signifying none-significance. When observing absolute differences between the two studies there seems to be a tendency towards growing difference of the 3-percentile with advancing age (figure 7)(39).

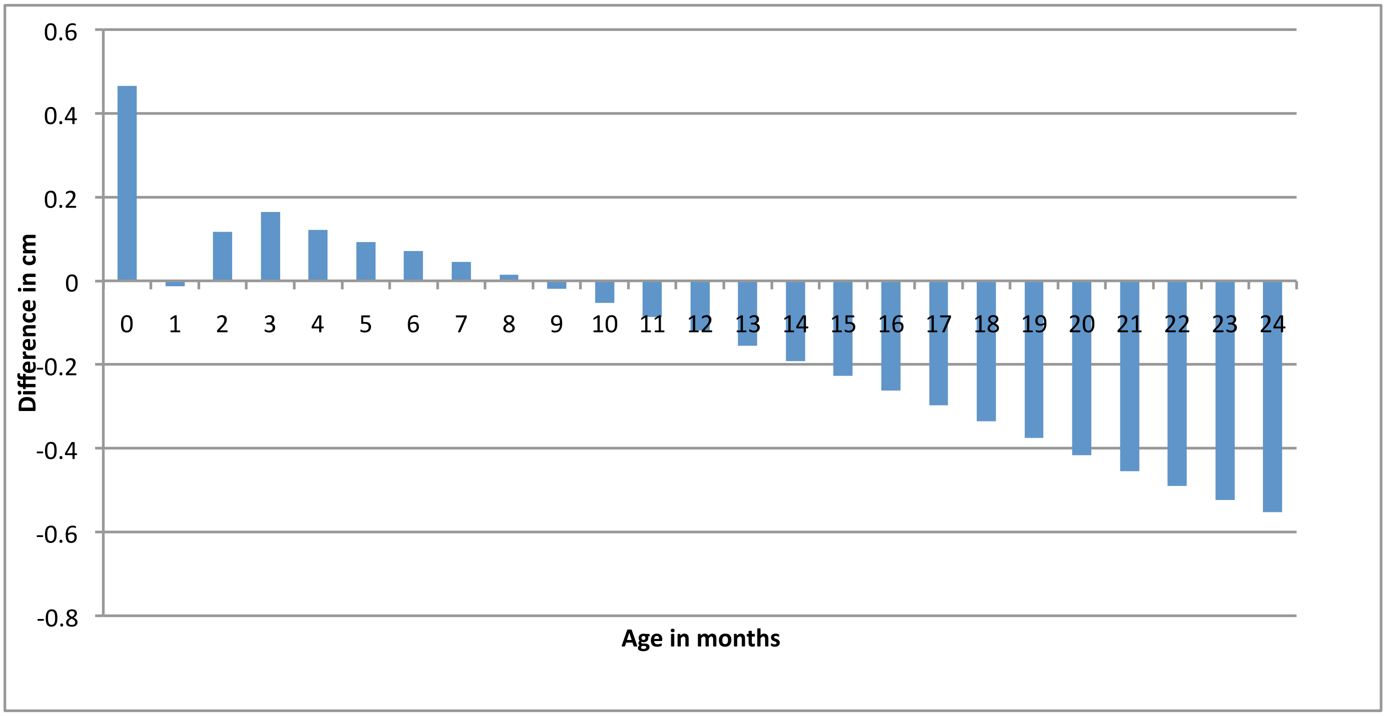


A

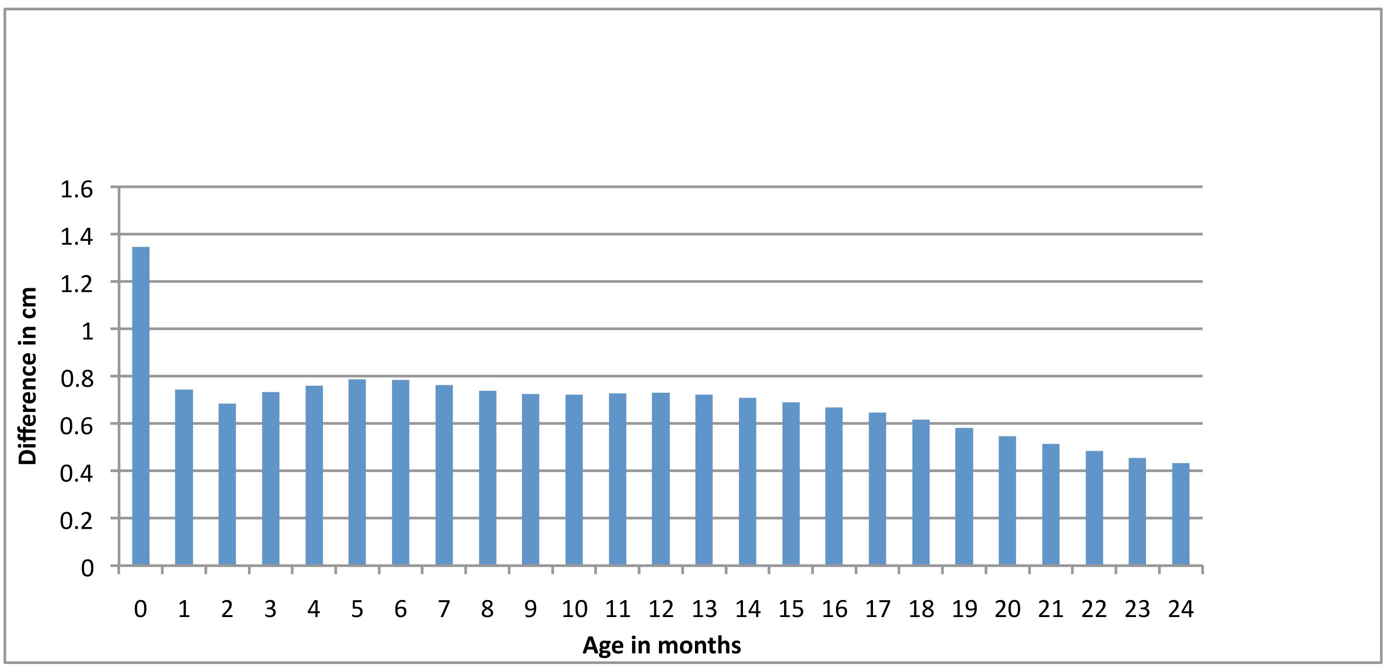


B

Figure 6. Percentile lines (97p, 50p, 3p) for Ethiopian (in black) with 95% confidence intervals (red) compared with the corresponding WHO percentiles (green), age 0-2years. A-girls, B-boys

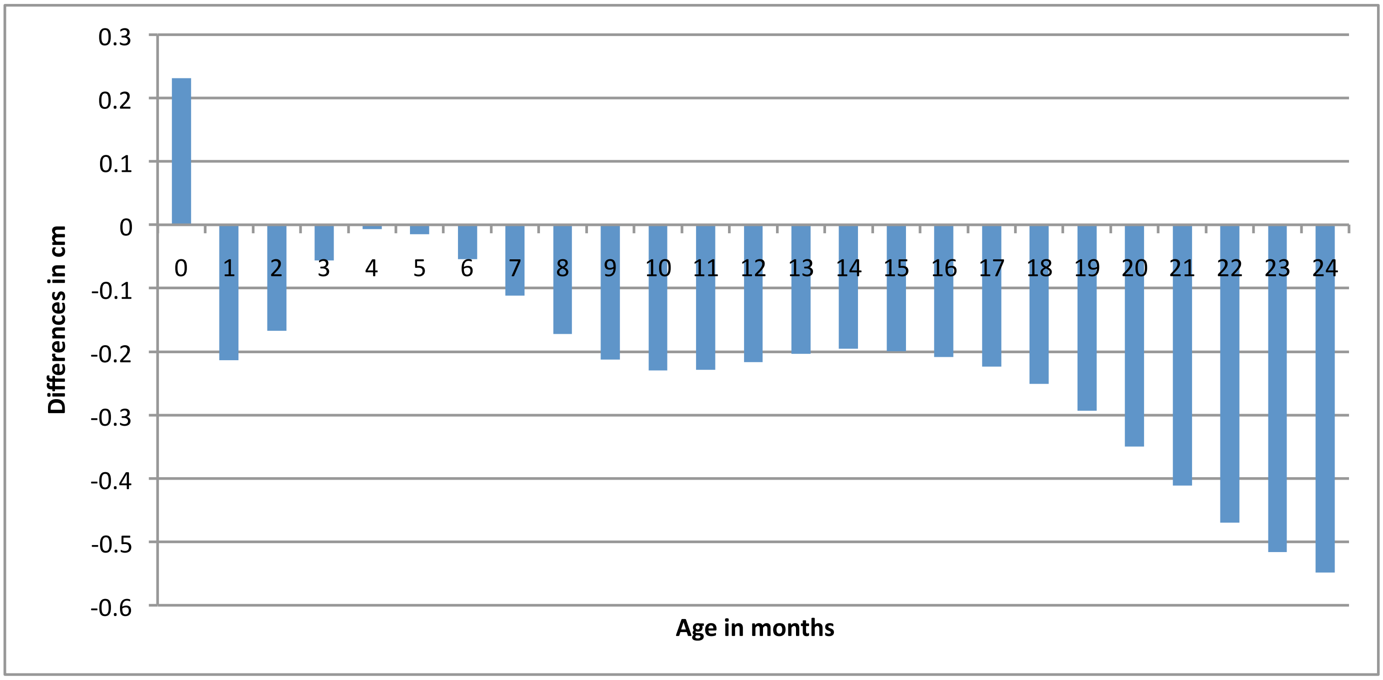


A

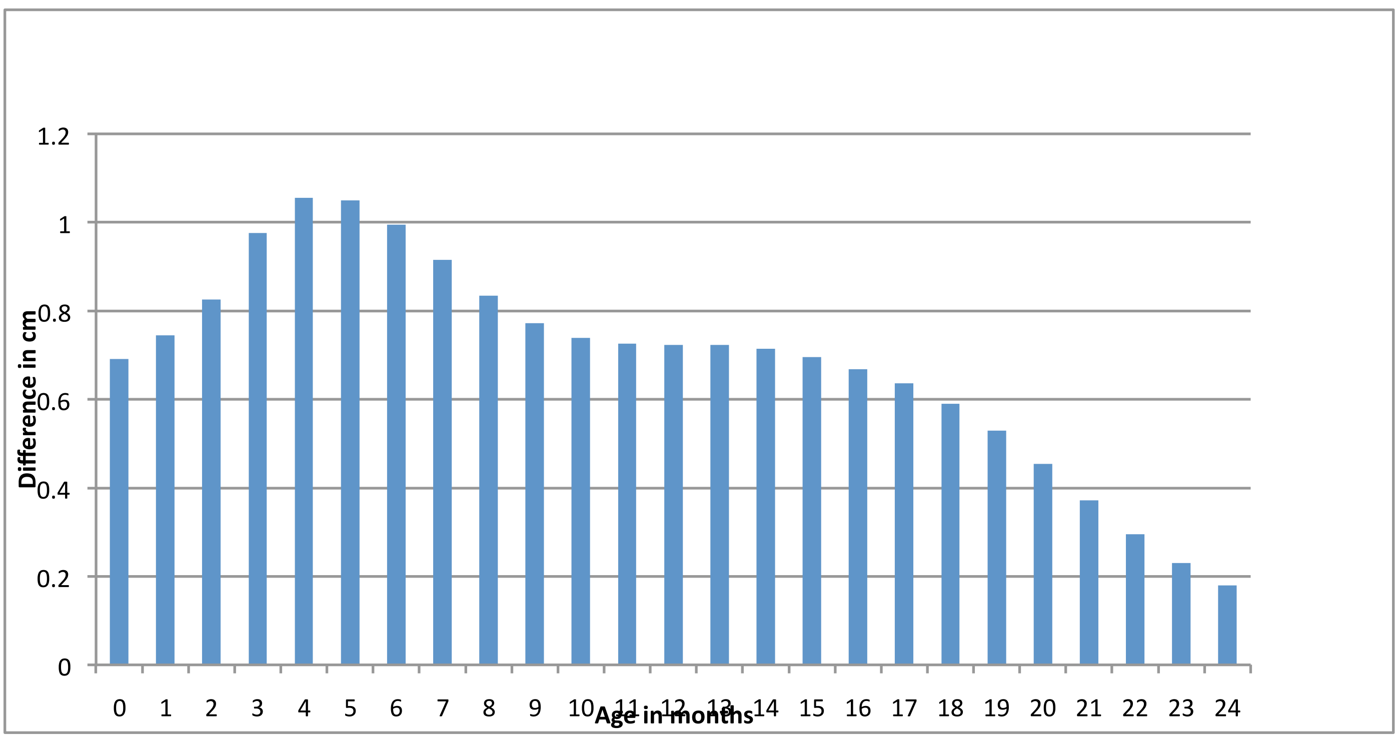


B

Figure 7. Difference (cm) between the Ethiopian and the WHO girls' curves for 3- percentile(A) and 97-percentile(B). Values above zero indicate that the Ethiopian measures are larger than WHO measures.



A

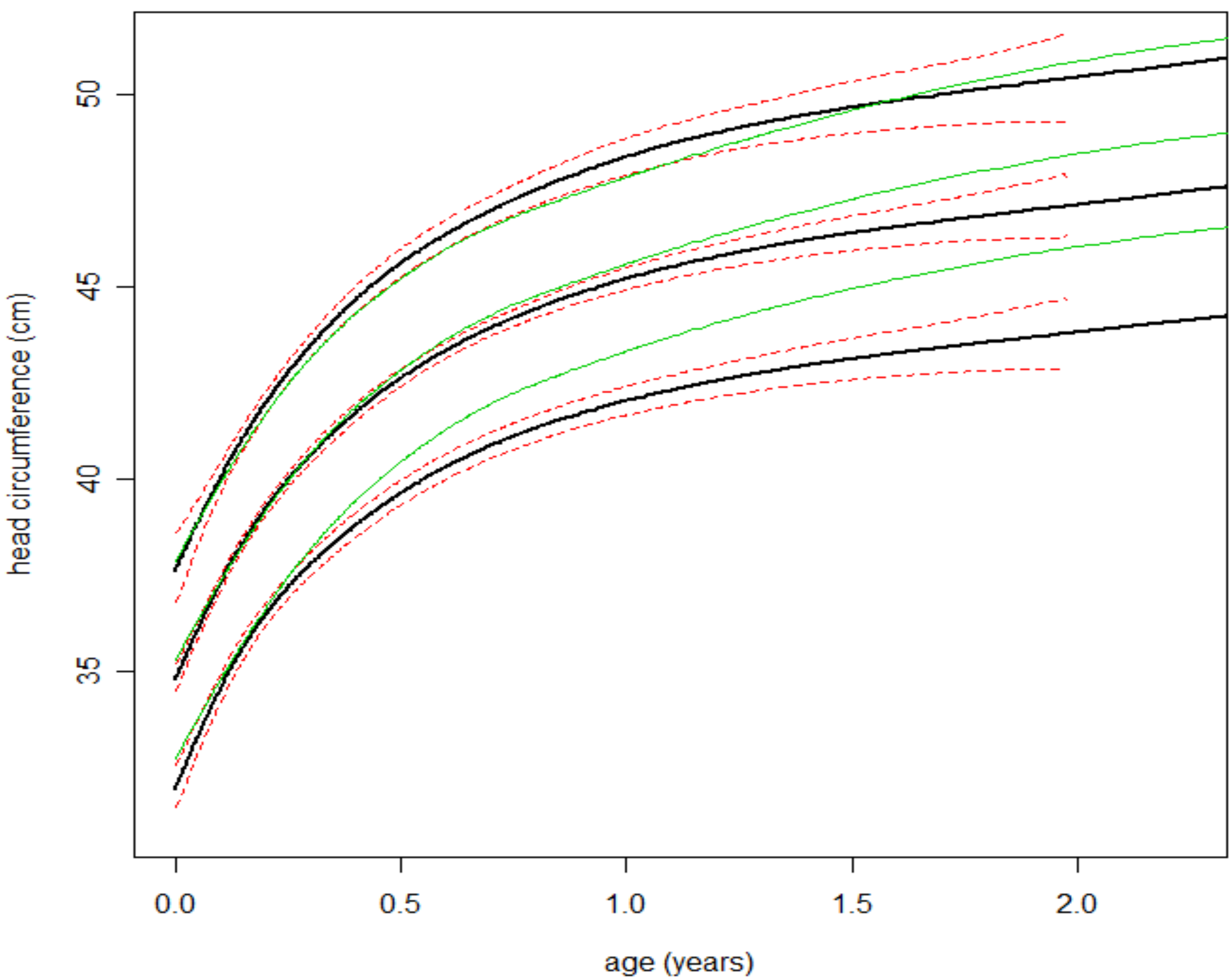


B

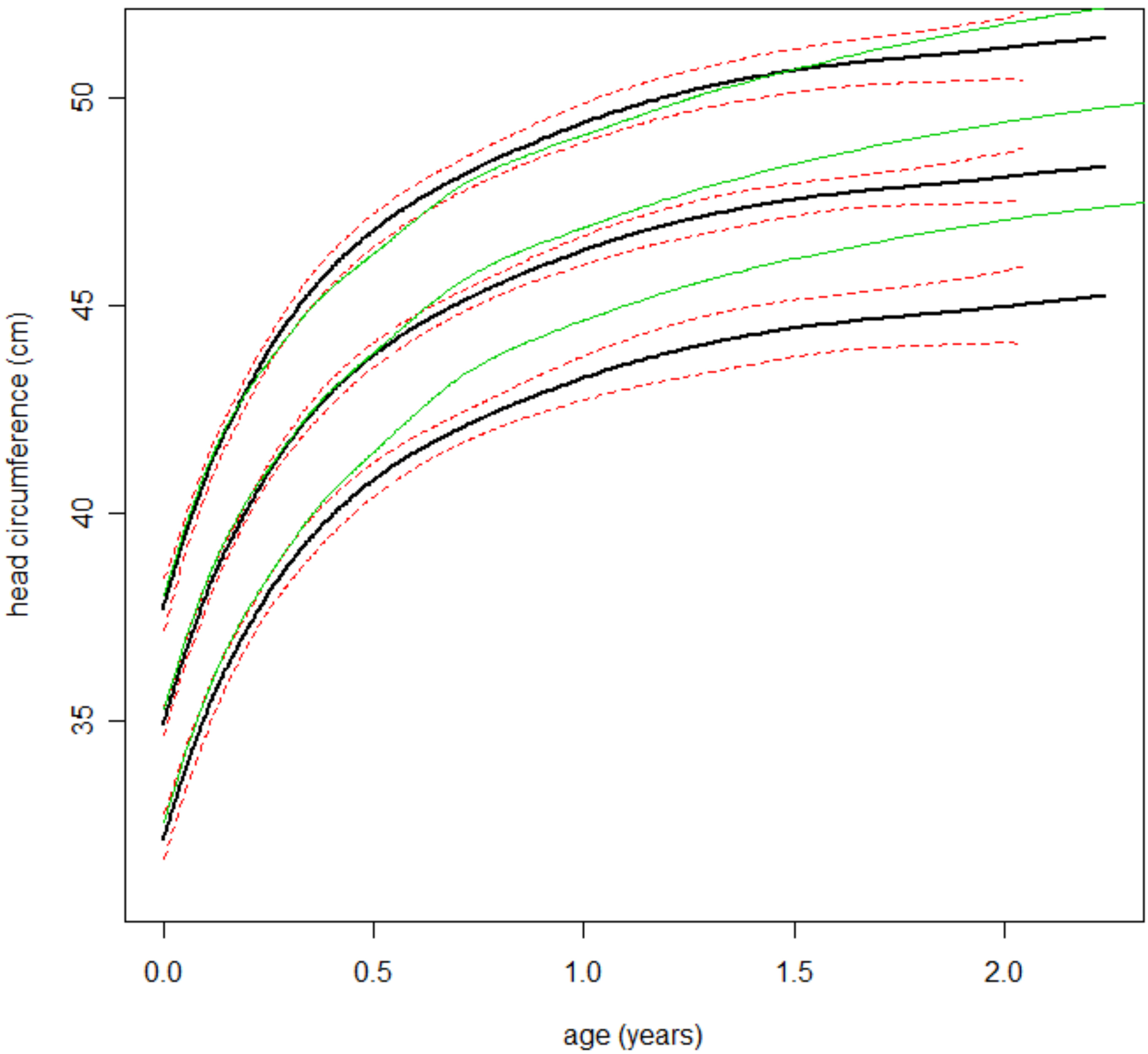
Figure 8. Difference (cm) between the Ethiopian and the WHO boys curves for 3- percentile(A) and 97-percentile(B). Values above zero indicate that the Ethiopian measures are larger than WHO measures.

Comparison of the Ethiopian curves with the Norwegian curves.

The HC growth charts for Ethiopia and Norway(30) in both girls and boys were also compared using the 3, 50, and 97 percentiles (Figure 9). We used the 95%CI for the 3-, 50-, and 97-percentile for our reference ranges but did not have the access to the corresponding values for the WHO study when assign visually the difference. Both the 97-centile and 50-centile are not different but the 3-percentile seems different, and juged from the absolute values (figure 10) increasing with age, the Ethiopian HC being increasingly smaller with age, for both sexes.

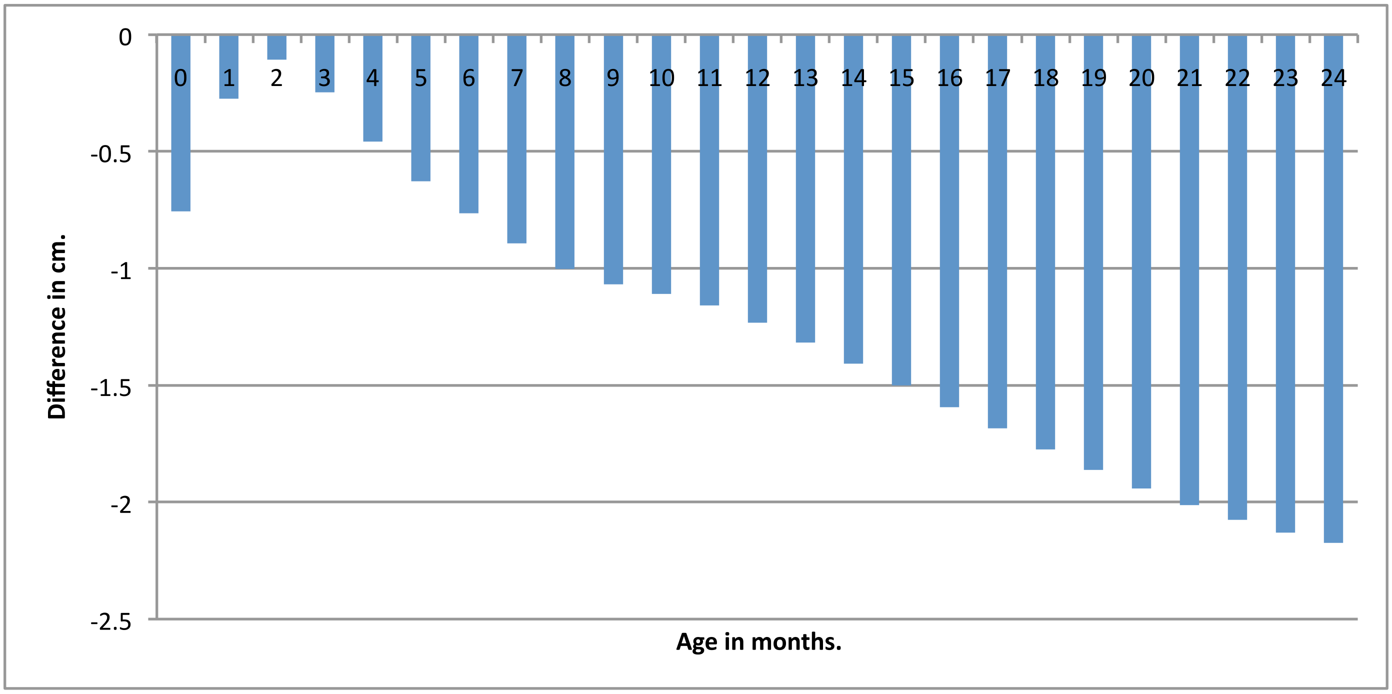


A

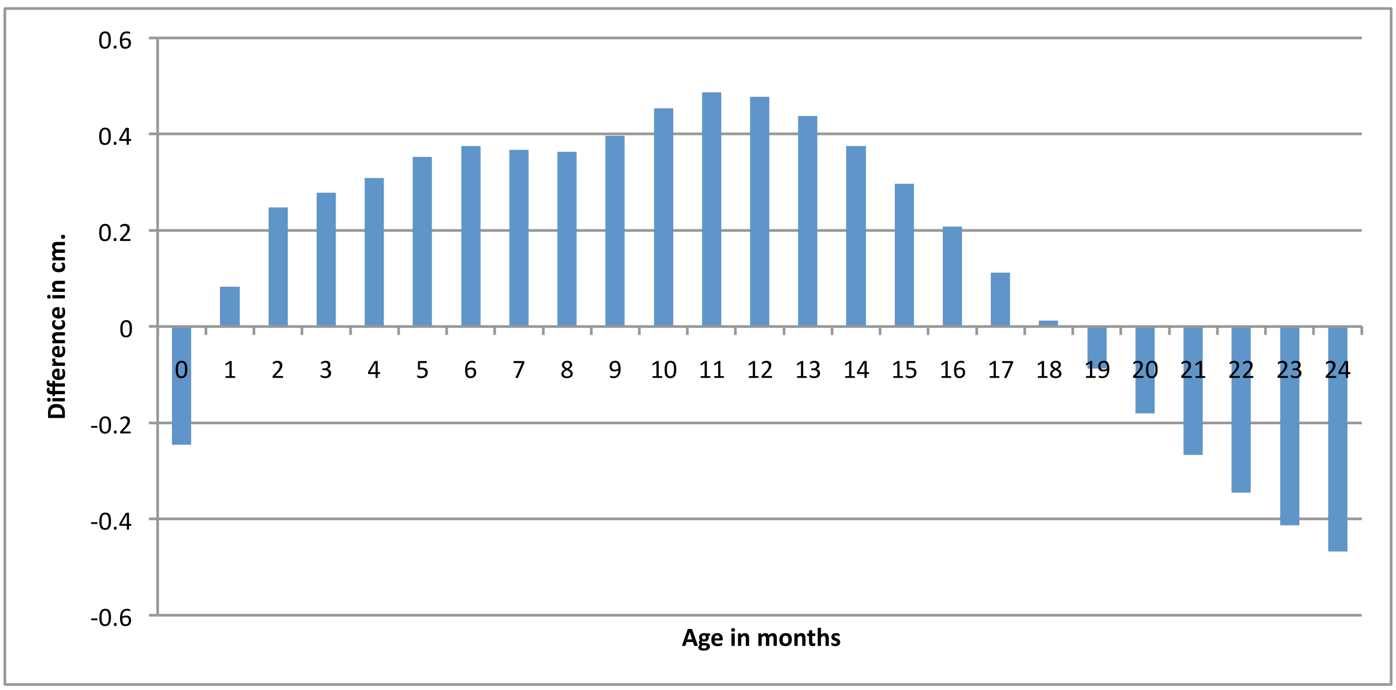


B

Figure 9. Percentile lines (97p, 50p, 3p) for Ethiopian (in black) with 95% confidence intervals (red) compared with the corresponding Norwegian percentiles (green), age 0-2years. A-girls, B-boys

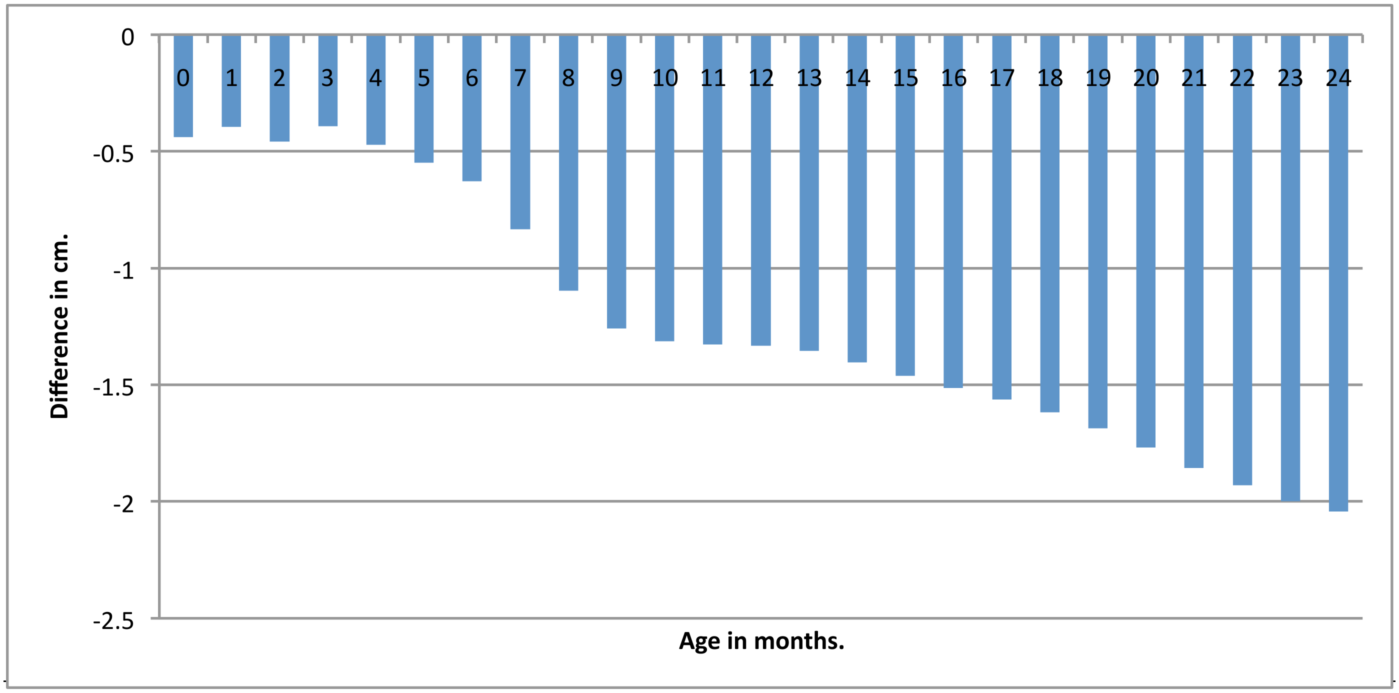


A

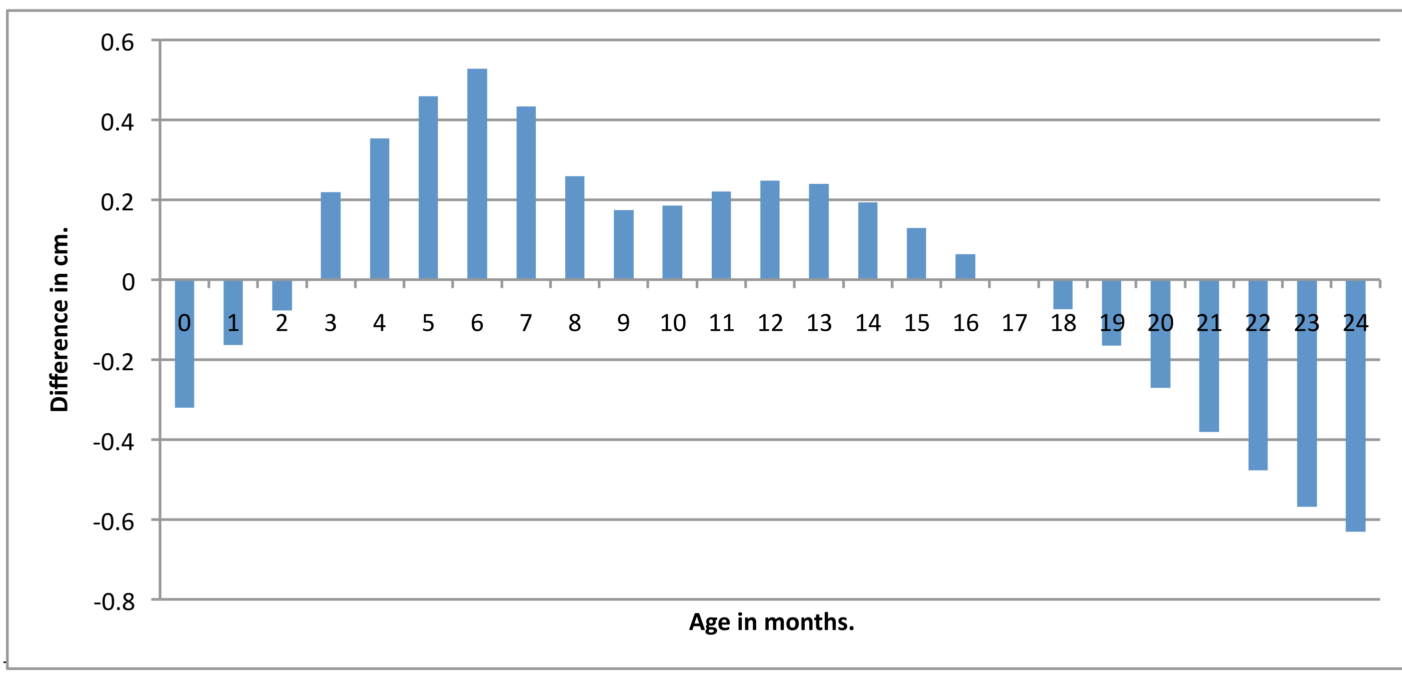


B

Figure 10. Difference (cm) between the Ethiopian and Norwegian girls' curves for 3- percentile(A) and 97-percentile(B). Values above zero indicate that the Ethiopian measures are larger than Norwegian measures.



A



B

Figure 11. Difference (cm) between the Ethiopian and the Norwegian boys' curves for 3- percentile(A) and 97-percentile(B). Values above zero indicate that the Ethiopian measures are larger than Norwegian measures.

5. Discussion and recommendation

In this chapter the researcher is going to discuss all the findings of the research that mentioned before. As the main objective of the study the HC standard for Ethiopian boys and girls based on the national data has been prepared. Comparison of this national standard was only for 3rd ,50th and 97th percentile. The first comparison is in between Ethiopian boys and girls HC. Based on the objective another important point of discussion is a comparison in between the existing standard (WHO) and this finding. Then we will come to the main point which is; weather is it needed to replace the WHO standard with the new national standard or not. As we are aiming the standard to be in use for early detection of hydrocephalus (big head) we also compare with nations such as Norway child population, which are on one extreme side of having large HC (40). Finally, we are going to discuss whether ethnicity has a factor for HC change or not.

The sex specific HC-for-age percentiles presented here are the first reference values from a nationally representative sample of Ethiopian children for the age range of 0-24month. As expected for both sex, in the first year of life head growth is more rapid than in the second year of life (41). The maximum range of HC in Ethiopian boys for the age group 0-1year is 11.40cm and in girls 10.42cm; whereas it is 1.75cm and 1.92cm respectively for boys and girls in the age group from 1-2yr. The same findings are seen in different studies. For the age group 0-1 year and 1-2 year, respectively, and in the order of first for boys then for girls: (9.5cm, 9.1cm) and (2.3cm, 2.4cm) (41); (11.6cm, 11.01cm) and (2.19cm, 2.29cm) (39); (11.72cm, 10.86cm) and (2.8cm, 3.06cm) (42); (12.32cm, 11.49cm) and (2.57cm, 2.54cm) (43); (11.56cm, 10.29cm) and (2.54cm, 2.86cm) (30). So as we see from all the above in early age (0-1yr) regardless of sex there is a high increment in HC. This is because a very fast histological change in this age (42). All this tells us measuring HC is extremely important and any deviation has to be watched more carefully in this age group than any age in the life time. And from all the above studies, we can see that the Ethiopian HC growth is almost the same to others in the first year of life for both sexes. But it is the slowest one of all in the second year of life.

Ethiopian boys HC in comparison with Ethiopian girls HC

The mean of HC for each age group and sex is indicated in table 1 and 2. For each percentiles (3^{rd}, 50^{th} , 97^{th}) the HC of boys is above girls. The minimal differences (0.19cm, 0.14cm and 0.09cm) for 3^{rd},50^{th} and 97^{th} percentile respectively and which are all at birth. The maximum difference for the same percentiles is 1.14cm (at 17month), 1.18cm (at 5month) and 1.21cm (at 5month) in the same order. So the mean difference ranges from 0.14cm to 1.18cm. This finding is in line with a published study by Barber(41) who gate the mean difference before the age of three years in the range from 0.79 to 1.17cm then the ranges decreases to be 0.45cm to 0.85cm. So we can say that at the beginning boys HC increases faster than girls then come to be slow but no where girls are above boys in HC (42). For all percentile with increasing age the gap in HC between boys and girls also increases. There is also a research which tells us that as there is a faster increase in HC of girls than boys in later age and this is more pronounced for HC than stature and weight (44).

Ethiopian HC in comparison with WHO HC

These have been presented with seven percentiles: 3^{rd} , 10^{th} , 25^{th}, 50^{th}, 75^{th}, 90^{th} and 97^{th}. But for simplicity as already mentioned the comparison is only for the 3^{rd} , 50^{th}, and 97^{th} percentile. For both boys and girls HC growth charts showed that the Ethiopian HC entirely lies above the WHO curve in the upper percentile. In this percentile for boys the difference ranges from 0.18cm to 1.06cm at the age of 24month and 4month respectively. In girls it is from 0.43cm at 24month to 1.35cm for neonates. So for the upper percentile in both sexes the maximum difference is more than 1percentile which is at an early age and the minimum in late age (24month). This tells us that irrespective of gender for the upper percentile with increasing age the WHO and Ethiopian curve close each other. For both sexes, we can also see from the 97 percentile graph the WHO curve is out of the 95%CI of Ethiopian curve and this difference might be statistically significant.

In both sexes, we have found that more Ethiopian children above +2SD and few below -2SD when using the WHO standard as a reference. The overall percentage above +2SD is 0.69% of each sex. While the percentage below -2SD is 0.21% for boys and 0.14%for girls. This result is consistent with a finding by Juliusson et al. (30) But more difference with WHO in Norwegian and Belgium standard than Ethiopian. So If one uses the WHO growth chart when measuring Ethiopian children, more children will be registered as having a HC above the 97^{th} percentile, although they are under the 97^{th} percentile of the Ethiopian population.

Regarding the 3rd percentiles the difference is very minimal compared to the 97^{th} percentile difference. Boys with a difference of 0.23cm in neonates to 0.55cm at 24month and for girls the difference ranges from 0.47cm to 0.55cm as the same age in boys respectively. So even if the Ethiopian is entirely below the WHO for the whole age span; they are almost on the same line up to the age of about 6-7mo. Since then the gap continuously increases and that could be explained by nutritional differences in between the two samples. But the WHO curves have never been out of the 95%CI of Ethiopian curve.

The period from birth to age two is especially important for optimal growth, health, and development. A WHO growth standard was prepared to show how all the world children should grow provided that they are exclusively breast feed (28). As described earlier in this paper Ethiopia is the most affected country by malnutrition in the world and when we see the overall trend of malnutrition in Ethiopian children it increases with increasing age, particularly in height for age (stunting/restricted height) and weight for age (underweight) (33). It is exactly at the same age of 6-8 month where the stunting, wasting and underweight level increases very fast and the Ethiopian HC starts go down from its comparisons WHO and Norwegians. Stunting and underweight keep going up where as wasting will go slightly down after having a maximum recording at the age of 9-11month(24). This could be by the difference in breast feeding practice in between these three samples especially in late age. In Ethiopia complementary feeding is not common, not introduced on time for all. Children aged 6-23months who are appropriately feed based on the recommendation is only 4 % in the country (33).

This is supported by a study which show that the rate of increase in HC is reduced for children who are severely deprived from malnutrition(45). A published study also supports this idea and show that protein energy malnutrition (PEM) in the early age group is a main reason for some damage to the brain and this may end up with a decrease in HC (46). A case control study of children under two years in Addis Ababa show that ” 35 of the 38 controls had a HC within the normal range, but 11of the 18 patients with marasmus had a HC below the normal range. The rest 7 of the patients with marasmus and all 10 of those with Kwashiorkor had a HC within the lower part of the normal range" (45).

Ethiopian HC in comparison with Norwegian HC

In the 97th percentile the difference is almost negligible (maximum of 0.63cm and 0.48cm for boys and girls, respectively) in which the Ethiopian is above the Norwegian. For both sex the two curves cross each other at the age of 17months where the Ethiopian standard starts to go down and then the gap continually increases. For both genders the Ethiopian 3rd percentile is entirely below the Norwegian standard with maximum difference recorded at 24mo age (2.04cm for boys and 2.17cm for girls) and minimum difference recorded at early age (0.39cm for boys and 0.12cm for girls). Here the maximum difference is not like in the 97th percentile, which was in between Ethiopian and WHO rather here it is in between the Norwegian standard and Ethiopian curve. The difference which is recorded in late age (24mo) reaches up to 2 percentile. This tells as irrespective of gender for the lower percentile with increasing age the Ethiopian curve going down while the other two curves (WHO and Norwegians) going up with the Norwegian the fastest. This could be explained by ethnic differences in addition to wide nutritional difference between Ethiopia and Norway.

When there is a large increase in HC particularly increases in each percentile level the first and the most important one which has to be considered especially in the first few years is hydrocephalus (47). At the lower percentile Ethiopian is the lowest of all. Later in 50th percentile Ethiopian curve become in between the WHO and Norwegian. But in the upper most percentile it is the Ethiopians which is the top one.

To sum up, Ethiopian reference ranges for children 0-24 months of age were found to be significantly different from those established by WHO, suggesting the use of local reference for the screening for hydrocephalus. We speculate that a trend towards lower 3-percentile values with advancing age in the Ethiopian children may be due to nutritional or environmental reasons.

Limitation and strength of the study

The study tries to collect data more from Addis Ababa and other big cities of the country.The ethnic distribution of the data is more or less as ethnic distribution in Addis in the sequence of Amhara, Oromo, Tigray, Somali and Gurage (table 3). In the 2011 census, more than 80 ethnic groups are listed, 10 of them with a population of more than 1 million It is therefore possible that the HC measurements should have been collected in several parts of the country in order to produce a HC curve that is representative for the whole population. However, Addis Ababa is only a little more than one century old and thus most of the inhabitants, relatively recently moved in from different parts of the country. The city is probably the area in Ethiopia with the highest ethnical diversity; thus, our HC charts are most likely created on the basis of data from an ethnically diverse population that do not deviate too much from the national average (table 4).the city seems to represent the different ethnicities nicely. Nevertheless, we believe that the strength of the chart would have been considerately improved if it were based also on measurements collected from all ethnic groups of the country. The children were screened only for nationality, ensuring that only children of Ethiopian origin were included in the HC-curves. The population of Addis Ababa has a total of less than 1 % of people from foreign nationalities, and none of the children in the study were among these.

As we see above PEM has an effect on the growth of HC, especially stunting (chronic malnutrition) and underweight. The prevalence of malnutrition in Ethiopian different in rural and urban areas. But as the HC data is collected from health centers and hospitals in the city this could be one potential limitation of the study. Another limitation of the study is not taking into account the gestational age of the mother, weight of the child, familial HC in which all the factors could have an effect on the HC of the baby. But different studies show that it is sex and age of the baby are the most determinant of HC growth.

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Annex

Annex 1 – Consent form

University of Bergen,

Center for International Health,
5021 Bergen,
NORWAY. Date of measuring: -----------------

Informed consent

Part 1: information sheet

Dear parents,

My name is Ephrem Biliigne Amare, and I am a Master student at the Centre of International Health at the University of Bergen, Norway. In collaboration with Addis Ababa University and by approval of the Ministry of health, this thesis aims to make a growth chart by collecting data from healthy children and that enables health professionals in the early diagnosis of hydrocephalus. Hydrocephalus means increased amount of fluid and increased pressure in the brain. If untreated, this can – sometimes – lead to health problems of the child. Through simple routine measuring of the head circumference this can often be detected. This procedure is common in many countries in the world. The data collection will be from April 2013 until November 2013 and around 3000 Ethiopian children under 24 months will be asked to participate in the study. If you agree to participate, I will measure the head circumference.
The measuring is **without harm or discomfort** for the child, and takes about half a minute, while the child is on your lap. It is as simple as measuring weight and height. It is no problem for me if the child is sleeping or in breastfeeding. If your child does not participate, you will still have the same service from the health center as before.

The information or measurement values of your child will be kept anonymous.

If you have any questions, do not hesitate to ask the responsible nurse at your local MCH-clinic.
They will eventually contact me and also you can call to me +251911945330

Part 2: Participants statement

Will you participate in the study:

Yes….. No….

Signature of parent/caregiver of the child:
Thank you for taking your time.

Kind regards,

Ephrem Bililigne Amare (sign.)

Annex 2

	Addis Ababa University College of Health Science Institutional Review Board	**SOP# AAUCHS 008** **Version 2.0** **Effective date: 1 Feb. 2009** **Page 13 of 13**
	Title: **3.2. Use of Study Assessment Form**	

ANNEX 3

Form AAUMF 03-008

IRB's Decision

Meeting No: 053/2013 Date (D/M/Y): August 7//2013

Protocol number: MFGC/058/07 Assigned No………………

Protocol Title: Head Circumference Development in Infants	
Principal Investigators:	Ephrem Biliigne
Institute:	AAU- CHS Department of Pediatrics
Elements Reviewed (AAUMF 01-008)	☑ Attached ☐ Not attached
Review of Revised Application ☐ Yes ☐ No	Date of Previous review:
Decision of the meeting:	☑ **Approved** ☐ Approved with Recommendation ☐ Resubmission ☐ Disapproved

I. Elements approved- 1. Protocol Version No. ……………………………………

2. Protocol Version Date………………………………

3. Informed consent Version No. ………………………

4. Informed Consent Version Date ……………………

II. Obligations of the PI-

1. Should comply with the standard international & national scientific and ethical guidelines
2. All amendments and changes made in protocol and consent form needs IRB approval
3. The PI should report SAE within 10 days of the event
4. End of the study, including manuscripts and thesis works should be reported to the IRB

III. **TO ESTM** ☐

Institution Review Board (IRB) Approval: Period from **August 14,2013** to **August 14,2015**

Follow up report expected in

3 Months ___ 6 months ____ 9 months_______one year____

Chairperson, IRB

Dr. Yimtubezenash W/Amanuel

Signature ______

Date: 14/08/13

Associate Director of Research and Technology Transfer

Signature _____________

Date ___________________

Institutional Review Board Office (IRB) Faculty of Medicine ADDIS ABABA UNIVERSITY

Annex 3

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Federal Democratic Republic of Ethiopia
Ministry of Health

ቀን 21 AUG 2013
Date
ቁጥር MOH/149/45/386
Ref. No.

To: Tigray Regional Health Bureau
Mekele
To: Amhara Regional Health Bureau
Bahr dare
To: Somalia Regional Health Bureau
Jijiga
To: SNNP Regional Health Bureau
Hawassa
To: Dire dawa Health Bureau
Dire dawa
To: Oromia Regional Health Bureau
To: Addis Ababa Health Bureau
Addis Ababa

Re:- ''Head Circumference Development in Infants'' PI- Mr Ephrem Bililigne Amare Co. PI Dr. Damte Shimelis.

Ephrem Bililgne Amare is a master student of international health at University of Bergen, Norway.

Addis Ababa University College of Health Sciences associate director for research technology transfer in its reference no. CHS/RTTO/052/13 dated August 19,2013 informed us the above project is going on since February 2008 G.C and need to collect more data from different parts of the country and ethnic groups.

Therefore we request your good office to write a supporting letter to health facilities.

With regards,

Megerssa Tadesse Negewo
Human Resource Administration
Case Team Coordinator

☏ 251-(0)11-5517011
251-(0)11-5515425
251-(0)11-5159869
251-(0)11-5518031

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✉ 1234
Addis Ababa,
Ethiopia

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In reply Please Refer to our Ref. No.