IODINE STATUS AND COGNITIVE FUNCTION OF MOTHER-CHILD PAIRS IN SIDAMA, SOUTHERN ETHIOPIA

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LIST OF ABBREVIATIONS

BMI	Body mass index
HAZ	Height-for-age Z-score
ICCIDD	International Council for the Control of Iodine Deficiency Disorder
IDD	Iodine deficiency disorder
T_3	Triiodothyronine
T_4	Thyroxine
Tg	Thyroglobulin
TH	Thyroid hormone
TSH	Thyroid stimulating hormone
UI	Urinary iodine
UIE	Urinary iodine excretion
UNICEF	United Nations Children's Fund
USFDA	United States Food and Drug Administration
WAZ	Weight-for-age Z-score
WHO	World Health Organization
WHZ	Weight-for-height Z-score

CHAPTER I

INTRODUCTION

Iodine deficiency is one of the most common micronutrient deficiencies and the single most common cause of preventable mental retardation and brain damage in the world. According to the International Council for the Control of Iodine Deficiency Disorders (ICCIDD), globally 2.2 billion people are affected by iodine deficiency which includes about 38 % of the world's population residing in iodine-deficient areas of Africa and East Asia (1, 2). Some estimate that across the world children at risk of inadequate intake of iodine account for about 285 million (3). Approximately 37 million newborns in the developing world still are born every year unprotected from iodine deficiency and its lifelong consequences (4) . The prevalence of iodine deficiency among school aged children is 36.4% in iodine-deficient areas worldwide (5). According to World Health Organization (WHO) estimates, about 350 million Africans live at risk of iodine deficiency with 28.3% affected by goiter, and 25% under the burden of disability caused by iodine deficiency as measured by disability-adjusted life years (DALYs). Iodine deficiency persists in Africa for reasons such as poverty, civil unrest, fragile political systems and malnutrition (6).

Ethiopia is among the high risk iodine-deficient countries in the East African region where iodine deficiency is prominent. It is a landlocked country in the Horn of Africa with a population of 73 million (7) where the major source of iodine is iodized

salt, which is the common method to combat iodine deficiency. The Ethiopian soil is low in iodine content. The staple foods in the study region were mostly plant-based. Several of these plant foods (kale, cabbage) contain substances that inhibit iodine absorption in the body (goitrogenic substances). This leaves the principal iodine source in the diet of the area to be iodized salt. The consumption of iodized salt in the area, which is only 18%, is the lowest among the regions of the country (8). Moreover, the use of iodized salt in the country as well as in the region showed a decreasing trend in recent years. A recent nationwide study (2007) showed this trend where the country as well as the region had very low percentage iodized salt use (the SNNPR iodized salt use was 2.2%) (9). The requirement for iodine is higher for the population groups directly involved in the process of growth. These groups include children and women of child-bearing age (10, 11).

In 2008, the Iodine Network reported that only 20% of households consumed iodized salt, leaving the rest of the population at high risk of iodine-deficiency diseases (IDD) (Figure 1.1). According to the report, the median urinary iodine concentration (UIE) was 58μg/L, the proportion of population with low UIE (<100μg/L) was 68.4% and the total goiter prevalence was 53% (12). Lack of access to iodized salt predicts increase in low iodine status in the population. This can be an indicator of increased prevalence and consequences of iodine deficiency. The highest consumers of iodized salt in the world are the households in the Americas with about 90% using iodized salt and only 10.1% prevalence of iodine deficiency (5).

Adequate iodine status in the community, especially for women of child-bearing age, is needed because iodine has tremendous effects on fetal brain development (13). The effects are most severe if iodine is deficient during pregnancy, but chronic deficiency

can also have an ongoing effect across all ages (6). Most affected are those suffering from the combination of fetal and postnatal deficiency that extends into childhood (13). Political will and strong law enforcement are required to sustain the availability of iodized salt to vulnerable groups of the community, children and women (6).

This project, thus, will target women of child-bearing age and their five-year-old children who are in the forefront of the most affected groups, because neonatal and postnatal development stages are crucial for brain development. Despite the effects of iodine on brain development, there is limited information on iodine status in the study area. This study was conducted in Sidama Zone in Southern Ethiopia. Southern Ethiopia is also known as Southern Nations, Nationalities and Peoples' Region (SNNPR). The SNNPR has thirteen Zones, eight special Woredas (counties) and ninety six districts. Sidama Zone is one of the thirteen Zones in the SNNPR (14). Thus this study will establish some baseline information about the association of cognitive function with iodine status in Sidama Zone.

Objectives

1. To assess the iodine status of women of child-bearing age and their five-year-old children.
2. To assess whether iodine status affects the cognitive function of women of child-bearing age and their five-year-old children
3. To evaluate possible relations between cognitive performance of mothers and children.

Hypotheses

H_a 1: The iodine status of mother-child pairs will be low.

H_a 2: Iodine status influences the cognitive function of women of childbearing age and their five-year-old children.

H_a 3: The cognitive test performance of mothers will significantly correlate to cognitive performance of their child.

Null hypotheses

H_o1: The iodine status of mothers and their five-year children will be in the normal range.

H_o 2: Iodine status has no effect on cognitive function of the subjects

H_o 3: The cognitive function of the mother has no relation to the cognitive function of her child

Limitations

The use of a convenience sample was considered a limitation depriving the chance to draw a representative random sample. Other limitations were absence of blood tests to further evaluate iodine status, language barriers (subjects were from four different tribes), and lack of an appropriate, quiet and private testing center. Time shortage was also another limitation given that the subjects had to travel to the test center from distant places and stay in the testing center for more than half a day for three days.

Significance of the Study

Iodine deficiency impairs physical growth and neurological development, which damages the brain to different degrees depending on its severity and on the stage of development at which it occurs in the life cycle of an individual (15). The outcome of iodine deficiency directly affects the health and the productivity of the individual, the economy and ultimately the development of the country. It is not a one-time damage and the consequences worsen if the deficiency continues to exist. If the future lies in the hands of healthy children, we can realize how iodine deficiency can hold back the development of a nation by decreasing productive potential.

Producers in Ethiopia have the capacity to iodize salt, and recently ten new salt iodizing plants have been built with an iodization capacity of 25% of the country's salt (2). However at present there is no monitoring system to enforce the legislation which requires iodization of salt sold for human consumption (16). Raising the level of awareness of the government as well as the producers and the consumers is very important with the sense of urgency to maintain the wellbeing of the population.

Availability of an adequate iodine supply to women before or during pregnancy would help to reduce the cause of childhood mortality by half and cretinism by two-thirds (10). To have the desired impact on the health of the community, all women of childbearing age should have access to iodine supplementation. However a recent nationwide study indicated that the study area (Southern Ethiopia) had the highest prevalence of total goiter rate among children (56%), as well as one of the lowest rates of iodized salt use (2.2%) and UIE (median 10μg/L and mean 31μg/L) (9). In another recent study in women of reproductive age (mean age at 31.8 (6.9)) the total goiter rate

was 35.8% in the country. The SNNPR had a goiter rate of 59.9%, the highest among the regions of the country (17). A target-oriented campaign of iodine supplementation programs and making iodized salt the only salt in the local market are some ways of securing iodine availability in the community (10) . Universal salt iodization could be accomplished at a cost of only 4 US cents per person per year eliminating iodine deficiency disorder in the process (2).

Labouisse, former Executive Director of the United Nations Children's Fund (UNICEF) wrote in 1978, “Iodine deficiency is so easy to prevent that it is a crime to let a single child be born mentally handicapped for this reason” (18). Nonetheless this crime persists. This project is initiated to establish baseline evidence which can be used to design intervention plans in the region before the consequence of the damage becomes worse over time. The socioeconomic and health development of most developing countries is put to test by iodine deficiency and it presents an ethical challenge to us all (2).

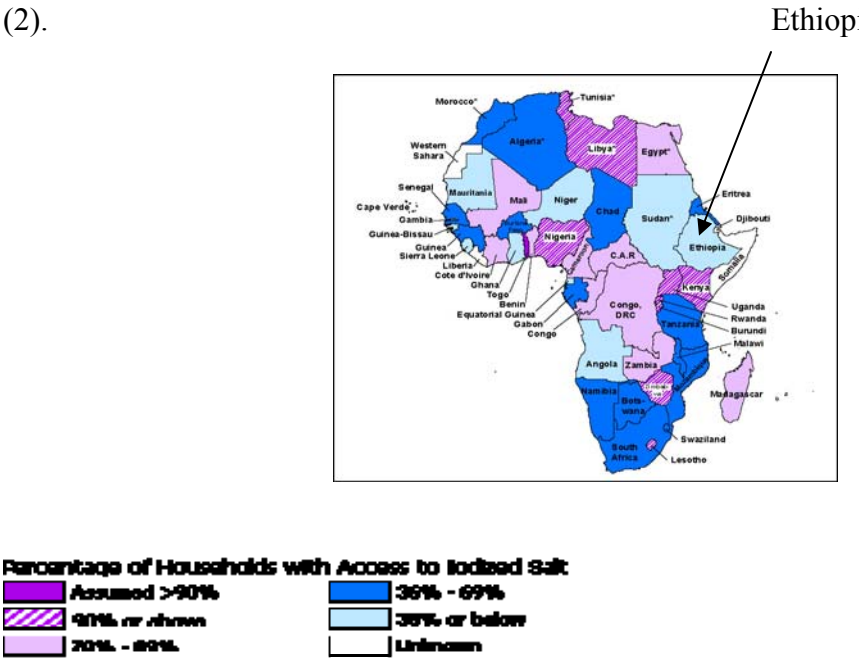

Fig 1.1. Percentage of households with access to iodized salt in Africa (1)

CHAPTER II

REVIEW OF LITERATURE

Introduction

In recent years, researchers in various countries have studied the effects and consequences of iodine deficiency on the mental and physical development of children and adults. Intellectual and motor development of different sections of a society have been studied in relation to iodine status (19) .

Iodine is a nonmetallic element belonging to the halogen family. It occurs in a variety of chemical forms, the most important being: iodide (I-); iodate (IO_3-), and molecular iodine (I_2). Most iodide is actively trapped by the thyroid gland where iodine (I_2) forms an essential component of the thyroid hormones, T_4 and T_3 (20).

Globally, iodine deficiency is one of the major causes of preventable mental retardation. It impairs physical and mental development, including intellectual capacity. Humans require iodine, a major component of the thyroid hormone. Thyroxine (T_4) and triiodothyronine (T_3) are forms of the hormone and have essential regulatory functions in the body (21). Failure to have the required amount of iodine may result in insufficient production of these hormones. This hampers the performance of different organs of the body, particularly muscle, heart, kidney, and fetal brain development resulting in a disease state collectively known as iodine deficiency disorders (IDD) (21).

Food Sources of Iodine

The primary source of dietary iodine is iodide, the dissolved form of iodine in sea water (10). The major source of iodine in most countries today is iodized salt. In addition, plants grown in soils containing adequate iodine, animals fed on those plants (grown in iodine-rich soils) and sea foods provide sources of dietary iodine. In many cases, the elements found in the plants are representative of the elements found in the soil where the plants grow. Mountainous or heavy rain fall areas are likely to be low in iodine due to erosion of the top soil, placing human and animal populations at high risk of deficiency (15).

Dietary Requirement

The iodine pool turnover in the thyroid gland helps to estimate the average requirement for T_4 in the body. This estimate was taken from various responses of serum thyrotropin concentrations to iodine intake. The proportion by weight of iodine in T_4 and T_3 comprises 65% and 59% indicating the importance of iodine in mammalian life. Biochemical reactions like protein synthesis and enzyme activity are mediated by the thyroid hormones in the major organs such as the developing brain, muscle, heart, pituitary and kidney (22).

The International Council for the Control of Iodine Deficiency Disorders (ICCIDD), World Health Organization (WHO), and the United Nations International Children's Emergency Fund (UNICEF) recommend the following daily amounts of iodine intake:

Table 2.1. ICCIDD, WHO and UNICEF daily recommended dietary iodine (23)

Population sub group	Amount
Infants and young children (0-59months)	90 µg/day
Children (6-12years)	120 µg/day
12+ years	150 µg/day
Pregnant and lactating	200 µg/day

For comparison, the 2001 US and Canadian recommended dietary allowance (RDA) from the Institute of Medicine is 150 µg/day of iodine for adults and adolescents, 220 µg/day for pregnant women, 290 µg/day for lactating women, 90 µg/day for children 1-8 yrs, and 120 µg/day for children aged 9-13 years. The adequate intake for infants 0-6 months is 110 µg/day and 130 µg/day for 7-12 months old (24). The upper tolerable level of iodine intake for an adult is 11,000 µg/day (22).

Absorption and Metabolism of Iodine

Though iodine is ingested in a variety of chemical forms, the complete reduction and absorption takes place in the gut. The widely used carrier in salt iodization is iodate which rapidly reduces to iodide and completely gets absorbed. After entering the circulation the iodide is primarily accumulated in the thyroid gland and the kidney. The thyroid, especially, concentrates iodide in large amounts for the synthesis of the thyroid hormones, T_4 and T_3. The remaining circulating iodine is excreted in urine. In addition to thyroid, the major organs of iodine storage are the salivary glands, breast, choroid plexus and gastric mucosa. The iodine concentration in the thyroid basal membrane depends on

a sodium/ iodide transporter. The sodium/ iodide transporter transfers iodide from circulation to a much higher concentration gradient of about 20 to 50 times that of plasma. This process assures the availability of enough iodine in the thyroid gland for hormone synthesis. In times of deficiency the majority of iodine stored in the thyroid gland is obtained from plasma (22).

About a teaspoon of iodine is the total requirement in a lifetime of an individual. However, the body doesn't have any storage mechanism for this amount of iodine in the thyroid gland (25) . Under normal circumstances more than 90% of dietary iodine is absorbed. In conditions where thyroxin is orally administered the bioavailability of iodine is about 75% (22).

The bioavailability of iodine in the body can be neutralized by certain foods. The value of dietary iodine can be reduced by vegetables from the Brassica or Cruciferae family such as cabbage, brussels sprouts, kale, broccoli, and cauliflower (23) , which upon digestion release thoicyanate and isothiocyanate (15) as well as foods like cassava, which contain goitrogenous substances and interfere with iodine absorption (26). Goitrogens are substances in some food groups which suppress the function of the thyroid gland and interfere with thyroid hormone (TH) production and absorption (22). Goitrogens affect iodine uptake by thyroid gland, the organification process or the release from the thyroid cells. Most of them act by competing with iodine in its active transport into the thyroid gland (26). Cyanoglucoside and thioglycosides are also naturally-occurring goitrogens. The cyanoglucoside is digested to release cyanide and converts to thiocyanate which inhibits the uptake of iodine by the thyroid. In addition to goitergenic

foods listed above, cyanoglucosides are present in foods like millet, lima beans, maize, bamboo shoots, and sweet potatoes.

Incidence of goiter and hypothyroidism were reported in infants consuming formulas based on soya flour. Addition of iodine to soya formulas prevented the development of goiter in the infants (22). Water from shallow polluted streams and wells also may contain humic substances that inhibit iodination in the thyroid gland. Unless there is a pre-existing iodine deficiency, the presence of goitrogens foods in the diet is not a major clinical problem (22). The presence of goitrogens is of public health concern in circumstances where both large quantities of these foods are eaten regularly and the levels of dietary iodine are low or marginal (27).

Physiological Function of Iodine

Even though iodine is only approximately 0.0004% of our total body mass, it plays a major role in metabolizing our food intake and determining our body's weight (19). Therefore the recommended daily allowance for the respective age groups is needed regularly (Table 2.1) (25) .

Thyroxin (T_4) and triiodothyronine (T_3) are forms of the thyroid hormone (21). The thyroid gland releases 100-125 μg of T_4 daily and small amounts of T_3 in a normal individual with an adequate iodine intake (28). In iodine sufficient areas, an adult thyroid contains about 15 mg of iodine (22).

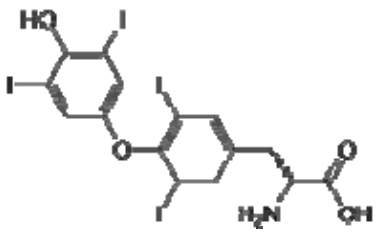

Fig 2.1. Structure of thyroxine (tetraiodothyronine, T_4)

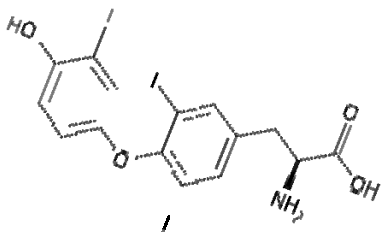

Fig 2.2. Structure of triiodothyronine (T_3) (29)

Iodine is involved in the making of TH, and thyroid hormone in turn regulates most of the metabolic patterns in the cells of the organism (30). For the secretion of thyroid hormones, the thyroid gland participates in a complex series of reactions. The vehicle used as carrier for iodine is the large glycoprotein molecule, thyroglobulin (Tg), which is synthesized inside the thyroid gland. The Tg and iodide meet at the apical surface of the thyroid cells where thyroperoxidase and hydrogen peroxide promote the oxidation of the iodide and its simultaneous attachment to tyrosyl residues inside Tg molecules. This procedure leads to the production of the thyroid hormone precursors, diiodotyrosine and monoiodotyrosine. The T_4 and T_3 in circulation are bound to proteins synthesized by liver such as thyroxin-binding globulin, transthyretin, prealbumin and

albumin. The rate of the binding is rapid in order to deiodinate T_4 into the more active forms of T_3 before migrating to target tissues (22).

Thyroid hormones regulate cell activity and growth in almost all tissues in the body and are, therefore, critical for both normal embryonic and postnatal development (15). Along with other iodine containing hormones, T_4 controls the rate of carbohydrate and fat metabolism (19). In the absence of iodine, production of other metabolic hormones is also impaired. As a result the body cannot utilize the energy from foods with the consequences of impaired physical and mental growth. Iodine is also involved in metabolic pathways of vitamins. For example, T_4 is required for the conversion of carotene from plants to vitamin A (19). The consequences of decreased thyroid hormone could increase levels of total cholesterol and low-density lipoprotein (LDL) cholesterol and potentially change the level of high-density lipoprotein (HDL) cholesterol (28).

Most importantly thyroid hormone is vital to brain development from pregnancy to the first two years of life, and if not available in sufficient amount it can be a cause of developmental damage in the brain (30). Continuous and severe deficiency of iodine at this particular stage of development affects thyroid hormone synthesis which results in hypothyroidism and impairment in brain growth with a clinical consequence of a range of mental retardation. The timed coordination of different developmental events through specific effects on the rate of cell differentiation and gene expression are also among the physiological functions of thyroid hormone (22, 30). During pregnancy thyroxin is available in the coelomic fluid beginning from the 6^{th} week in the first trimester before the fetus begins producing its own T_4, indicating the availability of T_4 from maternal source. The prenatal thyroid development begins at 10-12 weeks of pregnancy and

continues throughout pregnancy. About 20% to 50% of cord blood T_4 is obtained from maternal sources. The number of T_3 receptors and the amount of T_3 bound to receptors increases between the first and second trimester which is before the onset of fetal thyroid function (30, 31). The increase in the nuclear T_3 receptors and T_3 bound to these receptors by 6 to 10 fold between 10 to 16 weeks of gestation before the fetal hormone secretion is an indication of major fetal dependence on maternal sources of T_4 till mid gestation. Maternal thyroid hormone (TH) level in early pregnancy positively correlates with the infants' neurodevelopment as signified by subsequent outcomes. Though it is needed throughout the gestation period, the period of fetal life where TH is needed most is in the second trimester (31, 32).

One mechanism by which the thyroid hormone exerts action is through the binding of T_3 to nuclear receptors in the brain accountable for the expression of specific genes. The binding takes place during the fetal and early postnatal periods exactly in time with the development schedule of different regions of the brain. Thyroid hormone regulates specific brain genes through a complex nuclear receptor formation. In addition, at different stages of fetal development, T_4 regulates spatial and temporal gene activity in brain development. This is carried out by a range of signaling mechanisms (23, 32). The binding of nuclear receptors with triiodothyronine during fetal and early postnatal life is entirely dependent on local production of T_4 hormone from intracellular sources through the action of type II deiodinase, but not from circulating T_3 (30).

The major aspects of functional brain development in which T_4 plays decisive roles include: neurogenesis, neuronal migration, axon and dendrite formation, myelination, synaptogenesis and neurotransmitter regulation (31). Normal neural

proliferation, dendritic densities, synaptic profiles and transmission also depend on the availability of enough T_4. Insufficient TH at any one time during the fetal development can be a cause of significant brain damage (32).

The differentiation of photoreceptors, rods and cones including specific sub types of retinal oligodendrocyte precursor cells as well as production of essential proteins in the retina require sufficient amounts of TH. Absence of TH in an animal study resulted in impaired prenatal visual development and function. The earlier sufficiency is important for strong and persisting contrast sensitivity, though it is required throughout the term of the pregnancy. Normal contrast sensitivity function may account for the optimal visuospatial and visuomotor abilities in TH sufficient infants which otherwise could develop suboptimal abilities. To determine the effect of TH in the process of visual development, all causes of less TH in the growing fetus such as maternal hypothyroidism, congenital hypothyroidism (CH), and preterm birth usually associated with low TH, should be assessed (32).

Human Studies

A study was conducted in The Netherlands, which is an iodine sufficient country, on mental and psychomotor development in 220, 10 month-old infants. The outcome showed high risk of developmental delay for children from mothers in the lowest 10^{th} percentile of free T_4 at 12 weeks of gestation (other uncontrolled maternal factors, like depression, might account for the developmental delay as well) (33). Women with hypothyroxinemia, assessed around 12 weeks of gestation, gave birth to infants who had T_4 concentrations less than the 10^{th} percentile, and the infants scored very low in the

Neonatal Behavioral Assessment Scale compared with normal controls. These irregularities in behavioral scores are noticeable as early as 3 weeks of age in an iodine-deficient infant (23).

Assessment Methods for Iodine Deficiency

Measures of Iodine status

Three major parameters are used as indicators of iodine status in the effort to monitor and control iodine deficiency, and as important public health measures. The first is determination of urinary iodine excretion, the second, thyroid size and prevalence of goiter, and the third, determination of serum levels of thyroid stimulating hormone (TSH), T_4, T_3 and Tg. However, due to iodine deficiency adaptation of T_4 and T_3 in the circulating serum, they are less specific indicators of iodine deficiency. On the other hand, high values of serum Tg represent over stimulation of TSH and are a sensitive, index indicating the urgency of iodine deficiency. Regardless of serum concentration of TH, an elevated serum TSH, if not for other pathological reasons, indicates a shortage of T_3 receptors in the brain (23). Tg is the most abundant thyroid specific protein which is a key precursor in thyroid hormone synthesis and it does not have other known functions outside of the thyroid. Serum Tg is elevated as a reflection of TSH stimulation in time of iodine deficiency. Tg has been proposed as a better indicator of IDD in detecting thyroid function in response to salt iodization. It is a more sensitive indicator than T_4 or T_3 (34). In general iodine status is usually assessed by the most common methods, UIE, goiter size, and serum TSH or Tg.

Goiter Grading

Long term iodine status assessment can be done by goiter grading. Goiter is graded from zero to four based on the size of the enlarged thyroid gland as a result of iodine deficiency (35). Goiter grade zero is interpreted no goiter, goiter grade I_a is a stage where goiter is invisible when the neck is fully extended but thyroid gland swelling can be detectable by palpitation, goiter grade I_b is visible when the neck is fully extended. Goiter grade II could be detected from the swelling in the neck visible in a normal sitting position. Goiter grade III is a neck swelling visible from considerable distance, and goiter grade IV is a very large swelling also called monstrous goiter (35). Ultrasonography produces precise results in goiter grading. The use of ultrasonography is safe, practical, and easy to perform in the field. The reason goiter is an index for measuring longstanding iodine deficiency is that it is an indication of thyroid dysfunction which is manifested through a long period of time (23). Goiter grading is a poor indicator of iodine deficiency correction in children because of the long time required to detect normal thyroid functioning after universal salt iodization (5).

Urinary Iodine Excretion (UIE)

The median urinary iodine concentration differs according to the level of iodine in the body as a function of recent intake. Urinary iodine excretion is a good marker of very recent dietary intake and is an index of choice to assess iodine deficiency in a community to employ correctional measures. More than 90% of the iodine which is not retained in the serum iodine pool is excreted through urine. The remaining 10% is mostly excreted through the feces with small amounts lost through sweat (22). Urinary iodine values are

most conveniently expressed in terms of a range and median, or as the proportion of the population within a series of cut off points (23). In urinary iodine assessment, taking the population median is more relevant than taking an individual value or the group mean because the frequency distribution of the values is skewed towards elevated values (23, 36). A casual urine iodine concentration of individuals, including children and adults gives an adequate assessment of iodine nutrition for the population, provided the concentration is enough to analyze (23). To measure success of iodine supplementation in a community, urinary iodine concentration could be used as a primary indicator (37). According to the US third National Health and Nutrition Examination Survey (NHANES III), in areas of adequate iodine intake the urinary iodine concentration (μg/L) was 1.16 times the urinary excretion expressed in μg iodine/g creatinine (22).

The most common method for analysis of iodine in urine is recommended by WHO, UNICEF and ICCIDD. In this method the urine sample is digested with ammonium persulfate. Then the iodine concentration in the reaction is determined by its catalytic reduction reaction of cerium ammonium sulfate and arsenic acid in the solution. Potassium iodate is used as a standard. The result is quantified in the three ranges listed below, from 0-100μg/L as indicators of severity of deficiency (23). The iodine concentration in a 24 hr urine sample correlates with a casual sample obtained at any time of the day. The advantage of using casual samples is they are easy to collect and have been used as a major biological monitoring mechanism in the global study of iodine nutrition. The following formula can be used to estimate daily iodine intake based on urinary iodine and body weight.

= Urinary iodine (μg/L) * 0.0235 * Wt (Kg) = Daily iodine intake.

Example: the iodine intake of an individual weighing 57 Kg with urinary iodine of 100 µg/L will be 134 µg/L (22).

According to WHO, UNICEF and ICCIDD the severity of recent iodine deficiency is categorized in three groups in both adults and children: two more groups are identified as having high intake based on iodine excretion in the urine (30). Elevated values of urinary iodine (UI) show high recent intake of iodine from the diet or some form of iodine supplementation.

For UI the following categories are used (24):

- 0-19 µg/L indicates severe iodine deficiency
- 20-49 µg/L indicates moderate iodine deficiency
- 50-99 µg/L represents mild iodine deficiency
- 100-199 µg/L optimal iodine nutrition
- 200-299 µg/L more than adequate iodine intake
- >300 µg/L excessive iodine intake (36)

Iodine Content of Salt

The ease and cost effectiveness of iodizing salt makes it the best means for providing iodine to iodine-deficient populations. After 1990 the effort of ICCIDD to eliminate iodine deficiency by the year 2000 was accelerated. Sustaining the IDD control program has become a major focus all over the world. To achieve this goal, iodized salt distribution was chosen as a vehicle. Salt iodization is a more cost effective way of IDD

control compared to supplements and food fortification. The distribution of iodized salt costs 5-10 US cents per year per individual. In addition iodized salt is recommended as a supplement for IDD because of the fact that salt is used every day in the diet as a seasoning in all households irrespective of social and economic status or residential location. Usually salt production is carried out in specific locations making it appropriate for iodization and distribution control. Nevertheless this is not very practical in developing countries due to lack of iodization facilities and poor monitoring of uniodized salt distribution (23, 38).

Correcting iodine deficiency using iodized salt brought positive outcomes and significant reduction in brain development damage, mental retardation, goiter or thyroid dysfunction, and fetal morbidity. Water iodization is also efficient in controlling iodine deficiency in controlled and monitored situations but it is expensive to sustain as a national intervention program in poor developing countries (23). For fortification of salt with iodine, either potassium iodides or potassium iodates are usually used. The amount of iodine added to salt varies in different countries (1). For instance in the US the Food and Drug Administration (USFDA) recommendation is 60-100 mg KI/Kg of salt (39). The recommended amount of iodine in salt is a minimum of 40 ppm (40mg/kg) at production and 20 ppm (20mg/kg) at the consumption level. For comparison, in table 2.2 the concentration of iodine level used to iodize salt at production sites in different countries is presented.

Table 2.2. Iodine level used for salt iodization in some countries (1)

Country	Iodine Compounds used	Level of iodization at production level (mg Iodine/Kg salt)
Australia	Potassium Iodate	65
Cameroon	Potassium Iodate	50
Canada	Potassium Iodate	77
China	Potassium Iodate	40
Ecuador	Potassium Iodate	40
Germany	Potassium Iodate	25
India	Potassium Iodate	30
Indonesia	Potassium Iodate	25
Kenya	Potassium Iodate	100
Nigeria	Potassium Iodate	50
Panamá	Potassium Iodate/Iodide	67-100
USA	Potassium Iodate	77
Zimbabwe	Potassium Iodate	50 (at point of entry)

Impacts of Iodine Deficiency

Iodine Deficiency Diseases (IDD)

The ragged mountainous regions in the highlands of subsistence-based agricultural systems may have leached soil which deprives iodine to the plants and animals growing in the area. In these areas, the presence of goitrogens in staple foods such as cassava and millet further emphasize the effect of iodine deficiency accentuated by micronutrient deficiencies such as selenium. In communities where consumption depends only on home grown food items, children and pregnant women remain greatly affected by the consequences of iodine deficiency (6).

In 1983 the term iodine deficiency disorder (IDD) began to be used as representative of all complications caused by lack of iodine in the diet (40). All these developmental complications brought on as a result of iodine deficiency in a population

are grouped under IDD (30). After the coining of the term IDD, the International Council for Control of Iodine Deficiency Disorders (ICCIDD) was formed in 1985 to promote optimal iodine nutrition worldwide (38). The ICCIDD was founded by a group of experts and consultants to monitor, oversee and control iodine deficiency disorders at regional and international levels (6). Since IDD is a disease, handling the condition needs trained professionals in addition to basic preventive intervention programs at the community level (23). The most magnified effect of IDD as a public health threat is on socioeconomic under development of the population exposed to iodine deficiency due to lower intellectual performance as a result of brain damage (30).

A review by the ICCIDD in 1999 summarized the risk of iodine deficiency as follows:

1. About 38 % of the people in the world are at risk of iodine deficiency, which accounts for about 2.2 billion individuals
2. Around 130 countries out of the of 191 in the world are affected by IDD
3. About 740 million or 13 % of the population in the world have goiter
4. Among the at-risk population, only 68% use iodized salt at the household level (38).

Coordinating committees for the purpose of salt iodization exist in 105 countries with an action plan in 102 of them. Iodized salt legislation exists in 98 countries (30). In 2004, only 84 % of the 130 countries affected by IDD have national legislation or at least a draft on salt iodization. Though there was a marked decrease in the number of countries affected by iodine deficiency in the years 1993 to 2003, still, by the year 2006, 54

countries remained under the influence of the problem. The remaining countries are the poorest countries in the world with few or no laboratory facilities and limited technical skill to properly monitor salt quality in the iodization process (23). Despite the fact that IDD had been eliminated in several countries by universal salt iodization, control programs have weakened and IDD continues to exist (5). In spite of all the effort made to distribute iodized salt, obstacles remain to hinder reaching the target communities. Small-scale salt producers have made the salt iodization program very difficult in some countries. Some of them are unwilling to buy potassium iodate, which is the most common chemical used as iodine carrier, or they use much less iodine or carrier chemical than recommended. Lack of facilities for salt iodization, lack of proper monitoring mechanism on distribution and storage of the iodized salt and absence of laboratories for iodine status determination are among the factors aggravating the prevalence of IDD (40).

Though there are many newly established IDD control programs and lots of them have made progress in universal salt iodization introduction, iodine deficiency continues to be a major public health problem (31). The reason is that these programs can become fragile and need to depend on strong, persistent commitment from governments, donors, consumers and salt industries. The most important challenge in IDD control is ensuring sustainability in the fight against iodine deficiency (5). To consider a country not affected by IDD, the household iodized salt access has to be at least 90%, with median urinary values at about 100μg/L and the prevalence of UI values less than 50μg/L in not more than 20% of the population (23). If a community continues to live under iodine deficiency, it can lead to different health problems, ranging from mild intellectual and

psychomotor impairment to severe mental retardation, growth stunting, apathy, and impaired movement and speech or hearing. As summarized in Table 2.3, severe iodine deficiency doesn't only cause mental retardation and endemic goiter, but also higher rates of prenatal death and infant mortality (30). Iodine deficiency significantly raises the risk of stillbirth and miscarriage (2). Reproductive risks in ID include reduced rate of fertility and high incidence of first trimester miscarriage, still birth, anovulation and gestational hypertension. Populations living in iodine-deficient areas are certainly affected by some risk of brain damage leading to cognitive deficit in the area (38).

Table 2.3. The Spectrum of Iodine Deficiency Disorders (IDD)

Fetus	Abortions
	Stillbirth
	Congenital anomalies
	Neurological cretinism
	mental deficiency
	deaf mutism
	spastic diplegia
	squint
	Hypothyroid cretinism:
	mental deficiency
	dwarfism
	hypothyroidism
	Psychomotor defects
Neonate	Increased perinatal mortality
	Neonatal hypothyroidism
	Retarded mental and physical development
Child and adolescent	Increased infant mortality
	Retarded mental and physical development
Adult	Goiter with its complications
	Iodine-induced hyperthyroidism (IIH)
All ages	Goiter
	Hypothyroidism
	Impaired mental function
	Increased susceptibility to nuclear radiation

From Hetzel (1983) WHO/UNICEF/ICCIDD (2001) (41)

Hypothyroidism and goiter are common signs of iodine deficiency (42). Cretinism is the extreme case in which many of these abnormalities occur as a result of iodine deficiency early in life (15). Mothers in iodine-deficient areas suffer from cultural and socioeconomic consequences as a result of infertility, miscarriage or giving birth to mentally impaired children. The lifelong care and responsibility of a defective child will put pressure on her time as well as her resources. Thus, in most developing countries the consequences of IDD will have significant economic impacts on the family earnings (38).

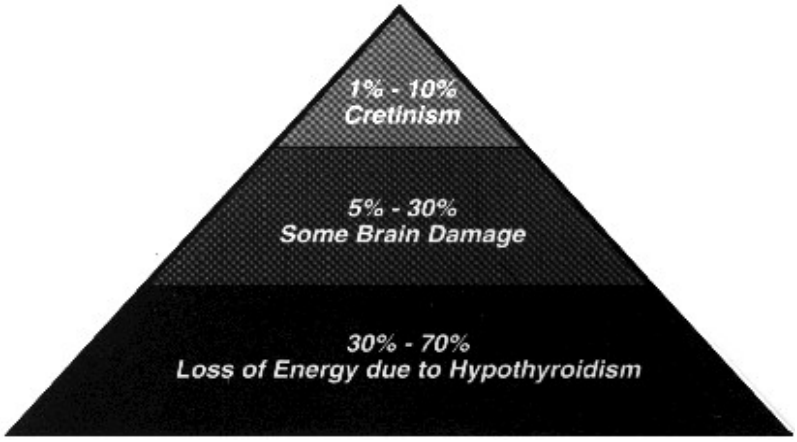

Fig 2.3. Percentage estimate of IDD damage caused by iodine deficiency in a community (1)

In an intervention study in western China, researchers treated irrigation water with potassium iodate (KIO_3) for several years. As a result in three treated villages, infant mortality rate decreased by half from the average infant death rate of the prior 5 years. In one village, infant death rate went down from an average of 58.2/1000 deaths in the past to 28.7/1000. In addition the odds of neonatal death were reduced about 65% in treated

villages compared to untreated villages (38). Another intervention study conducted in iodine deficient areas of Indonesia showed that treating infants 6-10 weeks old with oral iodized oil decreased mortality by half in contrast to that of the untreated group. These results were further confirmed in the Congo and Papua, New Guinea. In the Congo, women who received iodized oil in their 28th week of pregnancy had lower neonatal mortality rate and higher birth rate than those who had not received the treatment. In Papua, New Guinea a longitudinal study with a long-range follow-up showed children of mothers treated with iodized oil in iodine-deficient areas had significantly greater (15 yrs) survival rates than the untreated group. Despite the probability of the existence of other multiple confounding factors, correcting iodine deficiency evidently decreased neonatal and infant mortality (38). Most of the findings indicate that, in humans, iodine deficiency is more of a brain problem than a mere effect on the thyroid gland (30).

Table 2. 4. Recommended doses of iodized oil for the prevention of disorders induced by iodine deficiency

Duration of effect	Oral (mg iodine)			Intramuscular (mg iodine)
Age groups	3 months	6 months	12 months	> 1 year
Women of childbearing				
age (Non-pregnant)	100-200	200-480	400-960	480
Pregnant women	50-100	100-300	300-480	480
Infants - Children				
0 - 1 year	20-40	50-100	100-300	240
1 - 5 years	40-100	100-300	300-480	480
6 - 15 years	100-200	200-480	400-960	480
Males 16 – 45 y	100-200	200-480	400-960	480

Adapted from Delange, 1994 (43)

Hypothyroidism

Low concentration of thyroid hormone is termed hypothyroidism. The most common cause of hypothyroidism in the world is iodine deficiency. Some studies estimate the prevalence as 2- 5%. The percentage increase with aging could reach 15% by age 75 (44). Regions with dietary iodine deficiency are often affected by maternal and fetal hypothyroidism. It is believed iodine deficiency is always the cause of maternal and fetal hypothyroidism (31). Maternal hypothyroidism is one of the costs of iodine deficiency in the community. If the mother has hypothyroidism in the course of the pregnancy, the fetal brain might become susceptible to brain damage. Even the presence of mild or sub-clinical hypothyroidism caused by either mild iodine deficiency, or under replacement of TH during the course of the pregnancy is believed to affect and hinder fetal brain development (45). If left untreated, hypothyroidism can cause several complications in pregnancy outcome. The most common among these are preeclampsia, low birth weight, abruption placentae, and high risk of spontaneous abortion and prenatal mortality.

Fetal hypothyroidism, when severe and existing for longer duration, indicates the level of intellectual impairment (31). Hypothyroidism can damage the brain and the potential for intellectual development when it occurs as early as birth and even when it is transient. Thus in areas with significant hypothyroidism, early and sufficient iodine supplementation could almost entirely prevent fetal brain damage (30). In the case of maternal hypothyroidism, the effect becomes more prominent because of the fact that the fetus's own TH does not exist at the time it is needed most.

Hypothyroidism during fetal development could be permanent or transient. Transient hypothyroidism usually occurs temporarily when the mother is exposed to iodine-containing substances or when she has a history of thyroid disease. Transplacental passage of autoantibodies, drugs or immaturity of HPT (Hypothalamic-pituitary-thyroid) axis in preterm infants may also be causes of the transient type of hypothyroidism (31). Iodine supplementation during pregnancy could be a way to relieve the iodine deficiency stress caused by the high demand for the nutrient due to the many physiological needs for both maternal and infant thyroid function. Nonetheless, to check the neurocognitive improvements after the supplementation, further tests and study might be required (31). In addition to the neurocognitive damage, hypothyroid individuals suffer from a variety of adverse effects such as fatigue, loss of energy, lethargy, weight gain, decreased appetite, cold intolerance, dry skin, hair loss, sleepiness, muscle pain, weakness in the extremities, forgetfulness, impaired memory, inability to concentrate, menstrual disturbances, impaired fertility, decreased perspiration, blurred vision, diminished hearing, fullness in the throat and hoarseness. Insulin resistance is also one of the characteristic symptoms of hypothyroidism (44).

Human studies

A study conducted in the 1970's showed the effect of hypothyroidism and hormone replacement on IQ. Serum T_4 was tested by butanol extractable iodine (BEI). The BEI test is an estimate of thyroid function based on the amount of iodine bound to protein in the plasma. The result indicated 3% of the subjects (number of subjects= 1349), pregnant women from Rhode Island, were hypothyroxinemic (low BEI). The

children of these women had a mean IQ lower by 5 to 6 points at age 4 and 7 than women with sufficient iodine during their pregnancy. Furthermore at age 7, IQ of less than 80 was seen in 24% of the children from low BEI mothers compared to only 10% in controls. Thyroid hormone therapy appears to prevent further reduction in the IQ (31, 46).

A cohort study conducted in Morocco on children age 6-12 with severe iodine deficiency described the changes in thyroid function with iodine supplementation. At baseline the children were severely iodine deficient, median UI was 17μg/L and goiter rate was 72%. The children received iodized salt for a year before the distribution of iodized salt was discontinued because of logistic and financial constraints. The measurement of UI, TSH, T_4, Tg and thyroid volume, (Tvol) continued for 14 more months (5). UI and Tg had become normal with the mean Tvol decreasing by 34% and mean T_4 increasing one year after the introduction of iodized salt. However, the improvement seen with salt iodization came to a halt and thyroid function reversed rapidly with the discontinuation of iodized salt use. After ceasing use of iodized salt for just five months, the severity of iodine deficiency returned with the mean UI value at 19μg/L. The thyroid volume reduction was reversed entirely and the prevalence of hypothyroidism was much more pronounced than before the beginning of salt iodization. The median TSH and Tg became twice as high as the baseline values. Recurrence of IDD was characterized by a notable increase in TSH to normalize the amount of circulating thyroid hormone. Though most children in this study maintained a normal value of T_4 at 14 months after the cessation of iodized salt distribution, about 10% continued to be hypothyroid. The findings from the study in Morocco might not apply for adults because

children are more sensitive to iodine repletion due to smaller iodine stores and higher turnover in the body. The intra-thyroidal store of children is 10-20 mg. This study showed the vulnerability of children to iodine deficiency disorders during a short term lack of iodine in the diet or during termination of iodized salt distribution programs (5).

Hyperthyroidism

In individuals who are in a very severe iodine deficiency state and are suddenly exposed to a high intake of iodine, an adverse condition called hyperthyroidism or thyrotoxicosis may occur (6). Elevated levels of circulating free thyroid hormones, thyroxine or triiodothyronine or both, can result in clinical manifestations of hyperthyroidism. Iodine-induced hyperthyroidism occurs after administration of either supplemental iodine for deficient groups or pharmacologic doses of iodine given as medications in those with goiter (47). It results in the development of multifocal autonomous growth with scattered cell clones harboring activation mutations of the TSH receptors due to the increase in thyrocyte proliferation activated by iodine deficiency. Scanning with an X-ray showed some nodules in the thyroid have the capacity to store high amounts of iodine and become autonomous (43). Because of the many actions of thyroid hormone on various organ systems in the body, clinical signs produced by this condition are wide. In the elderly, the prevalence of toxic multinodular goiter increases with age and becomes the primary cause of hyperthyroidism (47).

A common feature of hyperthyroidism is weight loss caused by increased basal metabolic rate with a stimulation of lipolysis. In some cases up to 15% of weight loss was reported. Symptoms manifested due to elevated levels of circulating thyroid hormones

included chest pain, menstrual irregularity, nervousness, anxiety or emotional liability, heat intolerance, increased perspiration, weakness and fatigue among others (47).

Goiter

The volume of the lateral lobes of a thyroid gland is less than the terminal phalanges of the thumb of the individual under examination. If the volume exceeds the given measure, it is considered goitrous. When goiter is observed, the volume of the thyroid gland is at least four to five times greater than the normal size (48). The goiter may be diffuse or nodular in shape. When goiter starts to appear it is diffuse but as the severity continues it changes into nodular (22). The normal adult thyroid gland weighs 10-15 g with the two longitudinal dimensions of the lobe ranging up to 5 cm in length. Goiter is less frequent in men than women, the ratio is one to four (49). Iodine deficiency is the most common cause of goiter in the world. As suggested by the WHO, UNICEF and ICCIDD, where urinary iodine is greater than 100μg/l the prevalence of goiter usually is less than 5%. The WHO also approved these as normative values (48).

Worldwide over 600 million people have goiter (50). In Africa about 20% of the population, which is around 124 million individuals, are affected by goiter (51). The consequence of impaired thyroid hormone synthesis leads to increased TSH production, and this leads to increased cellularity and hyperplasia of the thyroid gland in the effort to correct the thyroid hormone secretion level. If the process continues, this results in establishment of goiter which is the enlargement of the thyroid gland (23). Thyroid size is a reflection of not only hypothyroidism but also hyperthyroidism. Excess circulating

iodine can impair intrathyroidal hormone production which leads to elevation of TSH and thyroid growth (22).

Goiter is not an adaptive process to iodine deficiency, rather it is a sign of maladaptation (23). To bring goiter rate as low as 5% in a community, children need to grow in iodine sufficiency. However, to correct goiter rate prevalence in children, the lag time of completion might take 10 to 12 years or more. In a community, if the school age children show more than 5% goiter rate, it is considered a public health problem (5). In most cases goiters are benign, and though they are less frequent in men, when found they are more likely to be malignant. Other than cosmetic deformity they are less likely to cause morbidity or mortality compared to other IDD (49).

Human studies

In a study conducted in 2004 in the southwestern part of Ethiopia on school children, the prevalence of endemic goiter was 27.4% (52). Likewise in 2000, a total of 2485 elementary school children were randomly selected from ten villages from four administrative regions in the country and were examined for clinical signs of goiter. Urinary iodine excretion was also assessed. The gross prevalence of goiter among school children was 53.3%. The prevalence was higher in girls (56.1%) than in boys (50%) (53). In a small study conducted in China on school children, goiter was reduced from 18 % to 5-9% after salt iodization for 18 months. It takes a longer period to correct goiter as a response to universal salt iodization due to several potential reasons, such as changing of old goiter to non toxic autoimmune goiter due to the presence of positive serum autoantibody (5).

In a controlled, double blind trial in the Boana area of the Huon Peninsula of Papua, New Guinea, correction of iodine deficiency using iodized oil (lipiodol) over a period of three years successfully prevented goiter. In a subsequent laboratory study in the same community, other researchers demonstrated the effectiveness of a single iodized oil injection (4ml) for correcting iodine deficiency for a period of as long as four and one half years (23).

Animal Studies

In a research trial, sheep were fed a low-iodine diet of crushed maize and pelleted pea pollard (pea stalk) (8-15 μg iodine/kg) which provided only 5-8μg iodine per day and an induced condition of severe iodine deficiency was created. After 140 days the fetuses were severely iodine deficient and were very different in physical appearance when compared to the control fetuses. The deficient fetuses had a reduced weight. Also, they did not have wool growth and had visible goiter, subluxation of the foot joints (partial dislocation of a joint), and deformed skulls. There was a delayed appearance of epiphyses in the limbs which resulted in delayed bone maturation. The symptoms were overt in the deficient fetuses with evidence of goiter and lowered brain weight and DNA concentration as early as 70 days. The complications continued and might be a result of reduction in cell number from delayed neuroblast multiplication which should occur from 40-80 days in sheep in a normal condition. Thyroid histology indicated hyperplasia started from the 56^{th} day of gestation, which was associated with a reduction of fetal thyroid iodine and a reduced plasma T_4 value (23).

Cretinism

In persistent severe iodine deficiency fetal brain damage can result in cretinism. Cretinism is the most serious of all iodine deficiency disorders characterized by brain damage which occurs very early in life (31). The estimate of cretins in severely iodine deficient communities is as high as one in ten. In most of these groups, thyroid enlargement is the earliest clinical feature. It is a reflection of an attempt by the thyroid gland to overcome the increased need for iodine as a consequence of iodine deficiency for thyroid hormone synthesis (22). The severity of the effect results in neurological cretinism which is manifested by mental retardation with mean IQ as low as 29, and impaired motor function with problems of movement (31). High prevalence of cretinism, which can reach up to 15% in a community, is termed as endemic cretinism (29). In addition to all other mentioned health impairments, motor rigidity, shuffling gait and signs of thyroid insufficiency with dwarfism, myxoedema and sexual immaturity are manifested in most cases (30). Cretinism is also characterized by spastic dysplasia or quadriplegia (paralysis of all four limbs) and afflicted persons are smaller in physique as adults (19, 30). Moderate iodine deficiency also caused impairment of intellectual development and definite abnormalities of psyconeuromotor function (30).

At the beginning of the 20th century, cretinism was described by Sir Robert McCarrison in north-western India. He listed all the symptoms of cretinism and mentioned that the patient usually had a goiter. He also described one type of cretinism which he called myxedematous, which showed severe hypothyroidism, short stature, and a very marked delay in bone and sexual maturation. In this type of cretinism goiter was not seen suggesting the patient's thyroid had atrophied. Deafness occurred only

sometimes. The second type of cretinism is endemic neurological cretinism which is characterized by three major features. When developed fully, it causes severe mental deficiency together with defects in the eye such as strabismus or cross-eyed, deaf mutism and motor spasticity, which disables the arms and the legs. In this case the mental deficiency was characterized by a noticeable destruction of the capability for abstract thought but visual development was not affected. Except in severe cases, the autonomic, vegetative, personal and social functions, and memory appear to be well preserved (23). The development of neurological features of endemic cretinism and a decrease in the growth of the fetal brain during pregnancy are outcomes of severe iodine deficiency where maternal T_4 is unable to saturate T_3 receptors in the nervous system (30).

According to De Long, the mechanisms underlying the observed clinical deficits in development are under-development of the cochlea as a cause of deafness, underdevelopment of the cerebral neocortex as a cause for mental retardation and underdevelopment of the corpus striatum as a cause of motor disorder (23).

The dysfunctions of the thyroid gland and the prevalence of goiter in cretins are similar to those observed in iodine deficient communities (23). Most cretins can walk because the function of hands and feet is preserved. This characteristic helps to differentiate from types of cerebral palsy which could exist in endemic areas (23). Among the types of cretins, the myxedematous cretin manifests a less severe degree of mental retardation than the neurological cretin. However both have all features of severe hypothyroidism which has existed since early in life. As in cases of nonrecognized congenital hypothyroidism, they show severe growth retardation, incomplete maturation of some organs such as the naso-orbital pattern, atrophy of the mandiable, puffy features,

thickened and dry skin, dry hair with no hair growth at times in eyelashes and eyebrows, and very much delayed sexual maturation. In this case goiter is absent most of the time without palpable lobes signifying thyroid atrophy (23). Therefore timely iodine supplementation in places of endemic cretinism is significant in the battle to reduce the adverse consequences of this deficiency (31). A controlled trial in the western highlands of New Guinea prevented endemic cretinism and reduced recorded fetal and neonatal deaths by giving iodized oil injections to mothers before pregnancy. This same injection had been shown to reduce established goiter after only one to three months (32)

Animal studies

In a study conducted in China, researchers fed pregnant rats a diet composed of maize, wheat, vegetables and water from Jixian village, a severely iodine deficient community with 11% endemic cretinism. The diet contained 4.5 μg/kg iodine. After the diet was fed to the dam for about 4 months, the neonate developed obvious goiter. Fetal serum T_4 was 3.6 μg/dL and brain weight was reduced compared to the normal controls whose T_4 was 10.4 μg/dL. The cerebellum exhibited delayed disappearance of the external granular layer with reduced incorporation of ^3H leucine in the deficient group, which was not seen in controls (23).

Interactions with Other Nutrients

Iron

Multiple nutritional and food related factors such as goitrogenic substances, malnutrition and deficiency of other micronutrients may affect the occurrence of severe

IDD and can also modify the mechanism of iodine prophylaxis (51). In addition, for effective prevention of IDD through iodine supplementation, the community has to be iron sufficient, because iron deficiency limits efficiency of iodized oil administration (23). The risk of neurological impairment and mental retardation in iodine deficient areas in most cases is due to combined effects of maternal, fetal and neonatal hypothyroidism and anemia (30). Thyroperoxidase, which catalyses the two initial steps in thyroid hormone synthesis, is dependent on iron. The effectiveness of iodine prophylaxis and thyroid metabolism in areas of endemic goiter has been shown to be affected by iron deficiency. Central nervous system control over thyroid metabolism and nuclear T_4 binding can also be modified by iron deficiency. Iron deficiency anemia not only limits the peripheral conversion of T_4 to T_3, but also reduces the concentration of T_4 and T_3 in plasma and increases the amount of the circulating thyrotropin.. Iron-sufficient children showed better retention response to oral iodized oil supplements than iron deficient anemic, goitrous children. Iron supplementation for goitrous children improved the effectiveness of salt iodization efforts. In one open and uncontrolled trial of iron treatment, goitrous anemic children showed improvement in their iodine status as a result of orally administered iodized oil (51).

Selenium

In addition to iodine deficiency, thyroid dysfunction in some areas is aggravated by selenium deficiency. The catabolism of T_4 to T_3 is also dependent on the presence of selenium. Selenium deficiency may cause impairment in the T_4 conversion to T_3. The selenium-dependent enzyme, I5'deiodinase is responsible for the peripheral conversion of

T_4 into T_3. The iodine from T_4 goes into the serum iodine pool or is excreted as urinary iodine. In places where sporadic congenital hypothyroidism exists, selenium deficiency can be involved in the process of thyroid atrophy causing neonatal and postnatal hypothyroidism. Central nervous system overload by way of follicular cell necrosis can also induce thyroid atrophy (22, 23). Selenium deficiency could increase the bioavailability of T_4 in the brain from maternal origin by preventing the catabolism of T_4 to T_3 during fetal development with a preventive role in early neurological damage (23).

Iodine and Cognitive Development

The major role of iodine in brain development makes it the world's greatest single cause of preventable mental retardation and brain damage in times of deficiency (30). Acute iodine deficiencies can affect an infant's intellectual, neuromuscular or psychomotor abilities (19). Most of the time iodine deficiency can be detected by visible goiter, however its damage can be manifested through impaired mental growth and development, which contributes to reduced school performance, intellectual ability, and work performance (4). The greater significance of iodine deficiency lies in the lower degree of mental impairment which occurs in almost all, otherwise normal, children in iodine deficient areas. Unless assessed carefully, this intellectual blunting could go unidentified (38). Most affected are those suffering from the combination of fetal and postnatal hypothyroidism that extends into childhood and adulthood (18). Among the organs of the body, the most susceptible to iodine deficiency is the brain. Brain development, especially maturation of the nervous system and myelination of nerve cells, requires the availability of iodine in the body (40).

The growth of brain has two periods characterized by maximal growth rate. The first is during the period from the first to second trimester, which is third to the fifth month of pregnancy. This period is characterized by the development phase in which neural multiplication, migration and organizations occur. Fetal thyroid function is not yet set, therefore the fetal thyroxine originates from maternal sources. The second phase of growth is in the third trimester to the second and third year of postnatal growth. This period is also associated with glial cell multiplication, and migration and myelination of nerve cells. At this stage the fetal thyroid hormone comes from the system of the fetus itself as it does with the child (23).

According to De Long, correction of iodine deficiency in the second trimester reduced neurological abnormalities, increased fetal head growth and improved developmental quotients in severely affected areas of Western China. Even though there was a general improvement in head circumferences and a slightly greater mean in development quotients after iodine supplementation in the later period of pregnancy, neurological development did not improve (38). In the second trimester, T_4 is responsible for somatogenesis of brain cells, neuronal differentiation, and formation of neural processes and is especially involved in the synthesis of the cerebral cortex, cochlea and basal ganglia. However, the third trimester is the period in which brain growth and differentiation occur (40).

In a meta-analysis of 18 studies involving 2214 subjects, children's iodine status and their mental performance were compared using standard intellectual tests. The researchers concluded that iodine deficiency reduced the mean intelligence quotient by 13.5 points. Non-diagnosed, less obvious disorders of cognitive and intellectual

development during infancy and childhood are more likely to be extensive and potentially make up a larger load on the economic outcome of affected communities (6). In light of the gravity of the problem, people living in iodine deficient areas are vulnerable to the consequential effects on the developing brain. For example in Sierra Leone, it is predicted for the five year period from 2006-2011, the productivity loss in the country as a result of the deficit in cognitive and intellectual development from iodine deficiency will exceed $42.5 million US dollars (6). These figures illustrate that iodine deficiency is a serious barrier to the development endeavor. Urgency in correcting this problem should not only be based on goiter treatment but neonatal mortality and the significantly lower IQ (40).

Human studies

The most commonly held argument is that the mental capacity of the growing child, once affected by iodine deficiency in early life, is impaired permanently (54). The pressing question is whether mental and psychomotor performance of children, while initially iodine deficient may still benefit from iodine supplements. In most cases iodine supplementation improved mental performance in children. In a double-blind, placebo-controlled study that examined the effect of iodine supplementation on the mental performance of Bolivian children aged 5.5-12 years, Bautista et al found no difference between supplemented and non supplemented children in performance on the Stanford-Binet and Bender tests. The supplemented group received an oral dose of 475 mg iodized oil (55).

In another study conducted in Benin, West Africa, among children aged 7-11 years, children with increased urinary iodine concentrations had significantly greater increases in performance on a combination of mental tests than did the group with no change in urinary iodine concentrations, suggesting a "catch-up" effect in terms of mental performance. The experimental group was given iodized oil (540 g I/L) before the experiment was discontinued due to the introduction of iodized salt in the area. The mental test batteries administered were block design, 5 tests from African Child Intelligence Test (Closure, Concentration, Exclusion, Fluency, and Maze), Hand movement from Kauffman ABC-II and Ravens Colored Progressive Matrixes (54). In a randomized double-blind placebo-controlled study conducted in southern Albania, moderately iodine-deficient school children supplemented with a single oral dose of 400mg iodine in the form of iodized oil, demonstrated improved information processing, fine motor, and visual problem solving skills (3).

Animal studies

In an animal study, pregnant marmosets (Callithrix Jacchus Jacchus) were fed a mixed diet composed of maize (60%), peas (15%), torula yeast (10%) and dried mutton (10%) obtained from iodine-deficient sheep. The newborn marmosets were iodine deficient and manifested sparsity in hair growth. The mothers as well as the newborns had enlarged thyroid glands with reduced plasma T_4. The thyroid gland size became greater in the second pregnancy with increasing severity of iodine deficiency. There was also a significant reduction of brain size in the second born which was not the case in the first pregnancy. The cerebellum damage was more outstanding in that in addition to

reduction in weight and cell number, there was apparent damage in terms of cell acquisition and histological changes. The study showed how iodine deficiency could significantly affect the primate brain too (23).

Cognitive Tests

Raven's Colored Progressive Matrices (CPM)

The Raven's (CPM) has been used as a test of intelligence in different cultures. It has been considered culturally fair for measurement of intelligence for children as well as adults. Recently Raven's CPM was used in several studies to determine fluid intelligence. It can test the ability to make comparisons and to reason similarity which estimates the ability to reason and solve problems. The test consists of 36 items in three categories, section A, AB and B each with 12 items. The tests are bright in color and arranged in order of difficulty (56, 57). The Raven's CPM is also considered easy to administer and to interpret. The board version of the test is more appropriate for children and for women who have not been to school. The person taking the test is expected to select the correct part of a diagram or design among six options to complete the picture or the pattern (3, 58).

K ABC-II Assessment (Kaufman Assessment Battery for Children)

The Kaufman Assessment Battery for Children -II (K-ABC-II) is a clinical instrument for assessing cognitive development. It measures mental processing and cognitive abilities. K-ABC-II is considered a culturally fair assessment tool. It measures abilities with little difference in scores between ethnic and cultural groups. These tests

give the opportunity to test people from different backgrounds. In addition they are easily understood, and ensure a child will not do poorly on them for reasons of clarity. The tests are classified based on what they measure and also further categorized based on age of the individual to be tested. In general the KABC-II tests measure:

- Learning (long-term retrieval); Storing and efficiently retrieving newly learned, or previously learned, information. These tastes are Atlantis, Atlantis Delayed, Rebus Learning and Rebus Delayed

- Sequential processing (short-term memory); Taking in and holding information, and then using it within a few seconds. It encompasses arranging information in a sequence or order to solve a problem with each input linearly and temporally related to the preceding item. These are comprised of Word Order, Number Recall and Hand Movement.

- Simultaneous processing (visualization); Perceiving, storing, manipulating, and thinking with visual patterns. Tests included are Rover, Triangles, Conceptual Thinking, Block Counting, Face Recognition and Gestalt Closure.

- Planning (fluid ability); Solving novel problems by using reasoning abilities such as induction and deduction. These skills are a function of biological and neurological aspects of development. These tests include Pattern Reasoning and Story Completion.

- Verbal knowledge (crystallized ability); Demonstrating the breadth and depth of knowledge acquired from one's culture. Verbal knowledge is measured by Riddles, Expressive Vocabulary and Verbal Knowledge.

The KABC-II consists of two types of batteries; a Core and an Expanded battery. The Expanded battery has supplementary subtests which help to increase the breadth of constructs that are measured by the Core battery. They evaluate psychological, clinical, psycho-educational, and neuropsychological features (59, 60).

In a study conducted in the Netherlands in 2003, researchers used KABC-II with children age 7y, to investigate the relationship between cognitive performance and long-chain polyunsaturated fatty acid (LCPUFA) levels. The study employed sequential and simultaneous tests. The results indicated that maternal intelligence and education were significant co-variables to the children's cognitive performance but not to the long-chain polyunsaturated fatty acid levels (61). The Hand Movements from the sequential processing was administered from the French version of KABC-II to school-age children in Benin after salt iodization in the study area. Children with improved UIE after salt iodization scored better in the test compared to the unchanged groups (54). For our study, age appropriate tests from Simultaneous, Sequential and Planning indices were used in addition to Ravens CPM.

CHAPTER III

RESEARCH DESIGN AND METHODS

Introduction

In the methodology section of this paper, the research team, the study area, subject recruitment and the study design will be discussed. Procedures of administering the household questionnaire will be included. The questionnaire included items on demographic, educational, and socio-economic characteristics as well as food frequency patterns. Anthropometric measurements, cognitive tests, collection and analysis of urine, and statistical analysis of the major outcomes will also be presented.

The Research Team

The research team, in addition to the principal investigator and the local advisor of the principal investigator, included a physician, three research assistants and three undergraduate students. Their duties included registration of the subjects, explaining the purpose of the study, recording the informed consent, conducting interviews with the women to fill out the questionnaires, taking anthropometric measures, conducting the cognitive tests, and handing out incentives to the subjects. In addition four translators and four community health agents worked in alternate shifts announcing door to door about subject recruitment, translating the content of the script and the consent to the

subjects and continued as translators throughout the study periods. The physician did goiter checks in both women and their children.

Training the Team

The procedure for the study was explained to the research assistants. Training was given to the undergraduate students, who later participated in conducting the cognitive tests. A two-day trial was conducted one day in the office and one more day in the research site along with the experienced research assistants. The translators were also given training of how they should explain the consent script and answer questions from the subjects.

Ethical Clearance

The study began after the Institutional Review Board of Oklahoma State University and the Ethics Committee of Hawassa University made a review of the human subject study protocol and gave permission to conduct the research.

Study Area

The research was conducted in the southern part of rural Ethiopia, Sidama Zone Wondo Genet Woreda from February to March 2007 (Fig 3.1). Sidama Zone is one of the 13 Zones in the Southern Nations, Nationalities and Peoples' Regional State (SNNPRS). According to data from the Sidama Development Corporation, the population in the Zone is estimated as 3.67 million. The majority of the population, about 85%, engages in agriculture as their main occupation. Population density in the Zone is 403 people per

square kilometer (62). Birth rate per woman in the Zone is 7.9 and Infant Mortality rate is 88 per 1000 live births (63). There are 54 clinics, 17 health centers, 21 health posts and only 1 hospital in the Zone. Health coverage was available for approximately 36% of the population in 2004 (14). Sidama Zone was selected as a research site because of absence of basic information on iodine status, high prevalence of visible goiter (visual assessment), and proximity of the area to Hawassa University the host institute for this project in collaboration with Oklahoma State University.

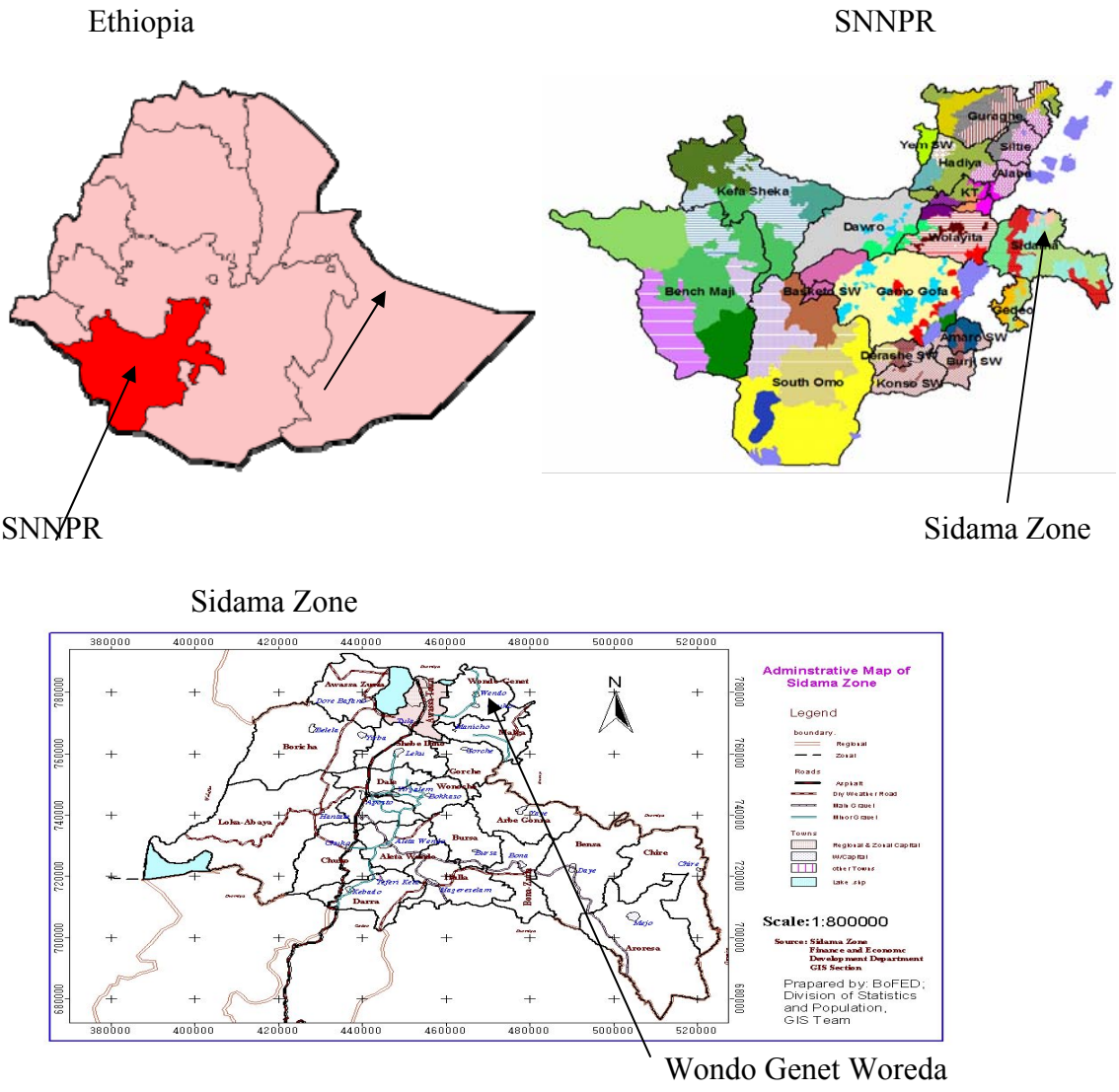

Fig 1. Maps of Ethiopia, SNNPR, the Sidama Zone and Wodo Genet Woreda

Study Subjects

Before recruiting subjects, the researchers made reconnaissance visits to the different local health and rural development offices to communicate the purpose and importance of the study. The local community leaders and health center heads were contacted and the purpose of the research was explained. The local community association, otherwise known as “Kebele” leaders, assigned local community health workers to participate in recruiting subjects. The enrollment announcement was made by the local community health workers through the local health center and door to door. Women with a 5 year-old child who wanted to participate in the research came on the day of the meeting to a local health center. Subject enrollment was made based on the inclusion/ exclusion criteria. All women who were pregnant or who had grade IV goiter were turned back.

A total of 100 women of childbearing age and their five-year-old children were enrolled to participate in the study. The purpose and the requirements of the research were explained to the women in the language they understood. The content of the script was read and explained to them by interpreters. Those who wanted to enroll in the study were given an appointment to come and give verbal consent which required recording of their name and number in a mini cassette recorder. The assent was also explained to the children. On admission to the study the subjects were given a code as an identifier.

The Study Design

The study was designed as a cross sectional study with a convenience sample of 100 women and their five-year old children.

Methods and Procedures

Considering the increased requirement of women and children for iodine and the detrimental cognitive effects of iodine deficiency, the following procedures were carried out to establish the occurrence of iodine deficiency of the study population.

Methods for Objective #1-3

Research Objective #1

1. To assess the iodine status of women of childbearing age and their five-year-old children.

Questionnaire Administration

Questionnaires about the household demographic, educational, and socio-economic characteristics, including housing conditions, water supply, sanitary and health service, food frequency and iodized salt use were administered (Appendices A and B). Questionnaires were translated from Amharic to the local languages the subjects speak during the interview.

Anthropometric measurements

Anthropometric measurements of weight and height for mothers and children were taken. The subjects were dressed in lightweight clothing while taking their weight and wore no shoes or head scarf during height measurement. Height was measured to the nearest 0.1 cm using a portable wooden stadiometer (Shorr Productions, Olney, MD) and weight was measured to the nearest 0.1 kg using a digital scale (Uniscale, UNICEF,

Copenhagen). The mean was calculated for each measurement. When the first two measures varied by more than 0.5 cm for height or 0.1 kg for weight, the measurement was repeated.

Goiter grading

A different day was appointed for the goiter checkup. The mothers and the children were asked to sit on a chair with their neck visible. The goiter grading was done by a physician from Hawassa University, Faculty of Medicine. Goiter was determined based on visibility and palpability. Zero represents no palpable or visible goiter. Grade I is palpable goiter with no visible goiter, grade II goiter is a visible swelling when the neck is in the normal position, grade III goiter is visible from considerable distance and grade IV goiter is a very large swelling of the thyroid gland in the neck.

Urinary Iodine Excretion (UIE)

A casual urine sample was collected from each subject for the determination of urinary iodine excretion (UIE). The collection was done after the cognitive tests were administered. The subjects were given a plastic cup and asked to collect about 10ml urine. The mothers were responsible for collecting urine for the child. Afterwards the research assistants poured the urine into micronutrient free polyethylene tubes and sealed and stored them in a refrigerator at Hawassa University until taken for analysis. The UIE was analyzed by spectrophotometer at the Ethiopian Health and Nutrition Research Institute (EHNRI) laboratory in Addis Ababa. The procedure used to determine the UIE was an accepted method employed by ICCIDD/UNICEF/ WHO (64). The reagents used

were standard iodine solution, 1µg iodine/ml in working dilutions of 20, 50, 100, 200 and 250µg I/L, chloric acid solution, sulfuric acid, 5M and 3.5 M used for dissolving ceric ammonium sulphate solution, arsenious acid solution and ceric ammonium sulphate solution.

Research Objective #2 and 3

2. To assess whether iodine status is related to the cognitive function of women of childbearing age or their five-year old children

3. To evaluate possible relationships between cognitive performance of mother and child.

A total of 12 tests were administered to test cognition of women and the children. The tests administered were the Raven's Colored Progressive Matrices, board version (for the mothers) and age appropriate tests from the Kaufman Assessment Battery for both the mother and child (KABC-II). The board version of Ravens CPM was used because it is more appropriate for children and for women who have not been to school.

The following KABC-II Assessment tests were administered to the women, which are primarily based on short term memory (Sequential), visual processing (Simultaneous) and fluid reasoning (Planning). Short term memory is where the subject is required to receive information and expected to use it within a few seconds. Visual processing involves perceiving information, storing it, manipulating and thinking with visual patterns, whereas fluid reasoning is based on solving problems using logic (59).

a. Number recall, Sequential processing

b. Word order, Sequential processing

c. Pattern reasoning, nonverbal, Planning

d. Rover, Simultaneous processing

e. Block counting, nonverbal, Simultaneous processing

The following tests were administered to the children

f. Conceptual thinking, nonverbal, Simultaneous processing

g. Triangles, nonverbal, Simultaneous processing

h. Pattern reasoning, nonverbal, Simultaneous processing

i. Hand movement, nonverbal, Sequential processing

j. Number recall, Sequential processing

k. Word order, Sequential processing

Data Analysis

The anthropometric measurements were converted to Z-scores using Epi Info child growth standard software (1978 CDC /WHO). Body mass index (BMI) for the mothers and height-for-age, weight-for-age and weight-for-height Z-scores for children were calculated. Data were analyzed by SAS version 9.1. Cognitive test results of mother-child pairs were evaluated by Pearson's correlation coefficient to look for associations among each cognitive test result, among groups of tests, goiter prevalence and UIE for both mothers and children. Frequencies, means, medians, standard deviations and correlations were computed for the of the study variables.

CHAPTER IV

IODINE STATUS AND COGNITIVE FUNCTION OF MOTHER-CHILD PAIRS IN SIDAMA, SOUTHERN ETHIOPIA

ABSTRACT

Introduction: Iodine deficiency is one of the most common micronutrient deficiencies worldwide and is a major cause of preventable mental retardation.

Objective: The purpose of this study was to assess the iodine status and cognitive function of women of childbearing age and their five-year old children.

Methods: One hundred women of childbearing age and their five-year old children participated in the study. The exclusion criteria were pregnancy or grade IV goiter. Demographic characteristics, food consumption patterns, anthropometric measurements, and iodine status were assessed. Cognitive tests including the Ravens Colored Progressive Matrices and tests from the Kaufman ABC-II battery were administered to both the women and their children.

Results: Mean (SD) age of the mothers' was 29 (6) y and family size was 7.0 (2.6). Mean maternal weight was 52.0 (6.8) kg and height was 159.3 (5.8) cm. Maternal BMI ranged from 15.3 to 29.0 with 14% of the mothers' having BMI <18.5. Occurrence of goiter was 85% in the women. Anthropometric assessment of children revealed 29% to be stunted (height-for-age *Z*-score <-2) and 12% to be underweight (weight-for-age *Z*-

score <-2). Cabbage and kale were among the more frequently consumed vegetables in the study area that could have been a source of goitrogens. Furthermore, only two households consumed iodized salt and no fish consumption was reported.

Goiter occurrence in children was 33%. Urinary iodine excretion for all participants was <49 μg/L, the upper cutoff value for moderate iodine deficiency. The cognitive test score ranges were wide and the majority of scores for all tests were very low for both mothers and children. There were significant correlations among individual test results between mother and child. Goiter and urinary iodine excretion (UIE) were significantly correlated to Sequential indices ($r= 0.39$, $p= 0.001$ and $r= 0.2$, $p= 0.05$, respectively), but not to Simultaneous indices for children.

Conclusion: The high prevalence of goiter and the low urinary iodine excretion demonstrate serious long- and short-term iodine deficiency in the study area. The results also show the existence of malnutrition in the community. The low iodine status might contribute to the low cognitive performance of the subjects. Efficient and cost effective methods to secure iodine availability in the community are urgently needed.
Key words: Iodine deficiency, Cognition, Iodized salt, Raven's CPM, Kauffman ABC-II, Goiter, Ethiopia.

INTRODUCTION

Iodine deficiency is one of the most common micronutrient deficiencies in the world. According to the International Council for the Control of Iodine Deficiency Disorders (ICCIDD), globally 2.2 billion people are affected by iodine deficiency which

includes about 38 % of the world's population residing in iodine-deficient areas of Africa and East Asia (1, 2). According to World Health Organization (WHO) estimates about 350 million Africans live at risk of iodine deficiency with 28.3% people affected by goiter, and 25% under the burden of disability caused by iodine deficiency as measured by disability-adjusted life years (DALYs). Iodine deficiency persists in Africa for reasons such as poverty, civil unrest, fragile political systems and malnutrition (3).

Ethiopia is among the high-risk iodine-deficient countries in the East African region where iodine deficiency is prominent. It is a landlocked country where the major source of iodine is iodized salt, which is the common method to combat iodine deficiency. In 2008, the Iodine Network reported that only 20% of Ethiopian households consumed iodized salt, leaving the rest of the population at high risk of iodine deficiency. According to the report, the median UIE was 58μg/L, the proportion of population with low UIE (<100μg/l) was 68.4% and the total goiter prevalence was 53% (4). In addition, a recent nationwide study indicated that the study area (Southern Ethiopia) had the highest prevalence of total goiter rate among children (56%), as well as one of the lowest rates of iodized salt use (2.2%) and UIE (median 10μg/L and mean 31μg/L) (5). In another recent study on women of reproductive age (mean age 31.8 (6.9)), the total goiter rate was 35.8%. The SNNPR had the highest goiter rate (59.9%) among the regions of the country (6). Lack of access to iodized salt predicts increase in low iodine status in the population. This can be an indicator of increased prevalence and consequences of iodine deficiency (7).

Iodine deficiency is one of the major causes of preventable mental retardation. It impairs physical and mental development, including intellectual capacity. Humans

require iodine, an essential trace element, as a major component of the thyroid hormone. Thyroxine (T_4) and triiodothyronine (T_3) are forms of the thyroid hormone and have essential regulatory functions in the body. Failure to have the daily required amount of iodine may result in insufficient production of these hormons. This hampers the performance of different organs of the body, especially the brain, resulting in a disease state collectively known as iodine deficiency disorder (IDD) (8). The central nervous system especially requires T_4 and T_3 for normal growth and development. Insufficient supply of thyroid hormone to the developing brain results in mental retardation and cretinism. A loss of 10 to 15 intelligence quotient (IQ) points could result from mild iodine deficiency. The continuation of brain damage and intellectual impairment can play a negative role in the educational and socioeconomic development of populations (9).

Adequate iodine status in the community, especially for women of childbearing age, is needed because iodine has tremendous effects on fetal brain development (10). The developing fetus is most severely affected if iodine is deficient during fetal brain development, but chronic deficiency can also have an ongoing effect across all ages (3). Most affected are those suffering from the combination of fetal and postnatal deficiency that extends into childhood (10). To sustain the availability of iodized salt to vulnerable groups of the community, children and women, political will and strong law enforcement are required (3). The objectives of this study were to examine the relationship between iodine status and cognitive function in women of childbearing age and their five year old children.

MATERIALS AND METHODS

Study Design

Sampling methods: A cross-sectional community-based study was conducted in Sidama Zone, Southern Ethiopia from February to March 2007. Purposive sampling was employed to select 100 women of childbearing age with their five-year-old children. Exclusion criteria were pregnancy or grade IV goiter. Contact was made with local health workers and community representatives to schedule a community meeting. The objectives and methods of the study were explained in local language. Consent was obtained from the women and assent was obtained from the children. Ethical approval for this study was obtained from the Institutional Review Board of Oklahoma State University and the Ethics Committee of Hawassa University.

Questionnaire: Data on demographic and socioeconomic characteristics, household food consumption patterns, and the use of iodized salt were obtained using a semi-structured questionnaire. Trained research assistants administered the questionnaire in local language through translators.

Assessment of Protein/Energy Status

Anthropometry: The height and weight of the women and children were obtained. The measurements were taken by a team of trained persons to avoid errors. The subjects wore lightweight clothing, no head scarf and no shoes during measurement. Height was measured to the nearest 0.1 cm using a portable wooden stadiometer (Shorr Productions,

Olney, MD) and weight was measured to the nearest 0.1 kg using a digital scale (Uniscale, UNICEF, Copenhagen). Measurements were repeated if the 1st two measures were more than 0.5 cm apart for height or 0.1 Kg for weight. For children Z-scores of height-for-age, weight-for-age and weight-for height were computed using the Epi Info software (1978 CDC /WHO). BMI (Wt (kg)/Ht (m^2)) for mothers was computed by SAS.

Iodine Status Assessment

Determination of Goiter: Sixty-seven mother-child pairs were evaluated for goiter. The goiter grading was done by a physician from Hawassa University Faculty of Medicine. Goiter grade zero represents no palpable or visible goiter. Grade 1 is palpable goiter with no visible goiter, grade 2 goiter is a visible swelling when the neck is in the normal position, grade 3 goiter is visible from considerable distance and grade 4 goiter is a very large swelling of the thyroid gland in the neck (11).

Sample Collection: Casual urine samples were collected by the participants. Both mother and child were given a micronutrient free polyethylene cup to collect about 10 ml of urine. The samples were stored in polyethylene tubes in a refrigerator at Hawassa University for future analysis.

UIE Determination: Urinary iodine concentration was determined by spectrophotometer using the method recommended by ICCIDD/ UNICEF/WHO (12). Urine was digested with chloric acid, and the amount of iodine was determined by its catalytic role in the reduction of ceric ammonium sulfate in the presence of arsenious acid.

Cognitive Tests

Kaufman ABC-II and Raven's Colored Progressive Matrices (CPM) (board version) assessments were used to evaluate cognition. The mothers' cognitive function was measured by Raven's CPM (board version) and Sequential (Number Recall and Word Order), Simultaneous (Block Counting and Rover), and Planning (Pattern reasoning) indices from KABC-II. The children's cognitive functions were measured using age-appropriate tests from the Kaufman ABC-II battery. These included Hand Movement, Number Recall and Word Order from Sequential, as well as Conceptual Thinking, Triangles and Pattern Reasoning from Simultaneous indices. Six research assistants were trained to administer specific tests. The analysis and interpretation of scores was done at Oklahoma State University.

Ravens Colored Progressive Matrices: Ravens Colored Progressive Matrices have been used to test intelligence in different cultures (13) . They are used to measure the ability to reason and solve a problem. The test is made up of three subsections of 12 visual problems each. The subject is required to select 1 of 6 choices to match a displayed pattern.

Pattern Reasoning: A series of pictures with linear patterns are presented with one section missing. The subject is expected to select the correct fit from four to six available options. It measures induction, general sequential reasoning and quantitative reasoning where solving problems using logic is required. The test is not timed.

Block Counting: This test is about counting the exact number of blocks in different pictures with stacks of blocks in them. It measures visual memory and spatial relations. The test is not timed.

Rover: Rover measures problem solving and following rules. It requires the ability to find the shortest or quickest way on a checker board with grids over rocks and obstacles to get a toy dog to a bone. It measures visualization, distance estimation and ability to engage in manipulative thinking. The test is not timed

Triangles: Several identical rubber triangles (blue on one side and yellow on the other side) are used to copy pictures from a book. This test measures measures visual memory and manipulating visual patterns. It is not timed.

Conceptual Thinking: This test is designed to measure reasoning and classification skills. The subject is shown pictures and asked to point to a picture that does not belong with the other illustrations.

Number Recall: In this test participants are asked to repeat several numbers after the examiner. These number series range from two to nine in length. Numbers are selected to have a similar number of syllables. The test measures short-term memory which requires storing information and using it in a few seconds.

Word Order: This test involves touching pictures of common objects in the same order as the examiner touches them. It measures short term memory which requires storing information and using it in a few seconds. The test is not timed.

Hand Movement: This test is conducted by showing a pattern of hand taps on a table and asking the child to repeat in the same sequence. It measures short-term memory which requires storing information and using it in few seconds (14).

Statistical Analysis

The data were compiled in Excel. Analyses were done using Epi info, and SAS, version 9.1. Epi Info was used because the new growth standards incorporated into the WHO 2005 Anthro program do not allow computations for children whose ages exceed 60 months. Frequency distributions, means, medians, standard deviation, ranges and correlations were calculated. Significance level was set at $P \leq 0.05$.

RESULTS

Demographic and socio-economic characteristics: The study population (n=200) included 100 mother-child pairs. Table 4.1 shows age, mothers' BMI and anthropometrics of mother-child pairs. The mothers' mean (SD) age was 29 (5.6) years. In 67% of the cases the family size was more than five people, the male: female ratio of the children in the study was 0.92. Tables 4.2 and 4.3 present the socioeconomic profile of the families of the subjects. In the two tables' educational status, animal ownership and land size are presented in detail. Forty eight percent of the mothers had never been to school. Though land ownership was high (76%), nearly 41% of the families had a small plot of land which was only about 500 to 1000 m^2. This land size is very low for a family whose main income is derived from farming.

In this study, families whose occupation was entirely farming were 56% and who partially engaged in farming were 20%. Animal ownership was also quite high (85%) and 76% of the study participants owned cattle. Most of the houses (94%) were made of mud and wood (Table 4.4). Only a few more than half of the respondents (57%) had

windows in their house. Tap water was the major source of water supply in the study area (78.8%) and 87% of the families had mosquito nets. Health service was available through local health centers and clinics in all cases.

Dietary Patterns: Animal product consumption was very low, only 19%, 4%, 1% and 1%, had egg, meat, chicken or fish per week respectively. Ninety one percent of the subjects had never consumed fish. Milk consumption (whole milk, buttermilk, cheese and whey) was better than the other animal products with 63% reporting daily consumption. Fruit and vegetable consumption was also low (18% and 33% daily).

Bioavailability of iodine can be reduced by certain plant foods containing goitrogens (15). Cabbage and kale which belong to these food groups were among the more frequently consumed vegetables in the study area and could be sources of goitrogens. The great majority used oil in their cooking daily (97%). Only 2% of the participants' households used iodized salt (Table 4.5).

Mother and child anthropometrics: Anthropometric measurements and their conversion to BMI or Z-scores are presented in Table 4.1 and Table 4.6. Mothers' BMI ranged from 15.3 to 29. Their mean BMI was 20.6 $\pm$ 2.4 and 14.4% of the mothers' had a BMI below 18.5 indicating the existence of malnutrition. Only 4.1% of the mothers were overweight (BMI of 26.6 to 29). The data show that in children stunting was 29% (Z-score <-2 SD) and underweight was 12% (Z-score <-2 SD). The mean Z-score for height-for-age was -1.3 and weight-for-age was -1.0.

Goiter grades: Sixty-eight mother-child pairs were checked for goiter. Goiter prevalence was 85% for the mothers and 33% for the children. The goiter grade distributions are presented in Table 4.7 and 4.8. One mother with goiter grade IV was

excluded from the study.

UIE results: UIE for all participants was < 49 μg/L. Ninety-nine percent of the mothers and 95% of the children had less than 20 μg/L UIE, the cut off point for severe iodine deficiency. Table 4.9 and 4.10 show the detailed UIE concentrations for both mothers and children. The median UIE was 1μg/L for both mothers and children.

Cognitive test results: The cognitive test results for the mothers and children are shown in tables 4.11 and 4.12. The range of scores was wide and the minimum scores for almost all tests were very low for both the mothers and the children. However Raven's CPM for mothers was significantly correlated with Sequential ($r=0.37$, $p=0.0002$), Simultaneous ($r=0.45$, $p< 0.0001$) and Planning ($r=0.4$, $p<0.0001$) indices from the Kaufman ABC-II. For the children, the Sequential index was significantly correlated with the Simultaneous ($r=0.49$, $p< 0.0001$) index.

Children were divided in two categories based on their anthropometric measures, <-2 Z and ≥-2 Z-scores. There were significant differences in cognitive test scores based on analysis of variance between stunted and non-stunted, and under-weight and normal-weight groups (Table 4.13). Scores on Word Order, Number Recall and Hand Movement (Sequential indices), Triangles, Pattern Reasoning and Conceptual Thinking (Simultaneous indices) and for the overall Sequential and Simultaneous indices were all significantly higher in the non-stunted group compared to the stunted group. Height-for-age Z-scores (HAZ) were significantly correlated to sequential ($r=0.40$, $p< 0.0001$), and simultaneous ($r=0.48$, $p<0.0001$) indices and weight-for-age Z-scores (WAZ) were also significantly correlated to Sequential ($r=0.39$, $p<0.0001$) and simultaneous ($r=0.48$, $p<0.0001$) indices. Although boys tended to be higher ($p=0.06$) than girls for the

Triangles test, sex difference of children was not a significant factor for all tests (Table 4.14). In addition, there was no significant difference in distribution of malnutrition, as measured by Z-scores <-2 Vs ≥ -2 Z HAZ, WAZ and WHZ scores, between male and female children. The mean and standard deviation for HAZ, WAZ and WHZ were also not significantly different between sexes (Table 4.15).

Regression analysis showed no significant contribution of maternal BMI to the cognitive test results from the Kaufman ABC-II; however maternal Raven's CPM was significantly predicted by mothers' education and latrine type (Table 4.16). The relation between education and cognition was consistent with previous findings about the link between education and adult cognition as measured by Ravens CPM (17). Level of education significantly affected the cognitive results of the mothers, except for Word Order and Number Recall (Table 4. 17). If mothers had ≥ 5yrs of education children had significantly higher cognitive test results. Table 4.18 shows HAZ, WAZ, WHZ, children's age, mothers' age and mothers' education as predicting factors for the child Simultaneous index ($R^2 = 0.42$). Stunting was a major predicting factor ($p<0.0001$). Likewise HAZ was a significant predictor for Sequential index ($p<0.0001$). However, child age, demographic and socio-economic variables such as family size and roof material also contributed to the equation as indicated on table 4.19. Tables 4.20, 4.21 and 4.22 present the correlation matrices for mother-child pairs and for other variables in the study to mothers' and children's cognitive test results. Mothers' education was significantly correlated to the mothers' cognitive test results in most cases. In addition household heads' education (husbands in 92 % of cases) also significantly correlated to mothers' cognitive test results as shown in table 4.20. In the case of children in addition

to malnutrition indicators and mothers' education, household head's education was also significantly correlated to children's cognitive test results (Table 4.21 and Table 4.22).

Correlation of cognitive test results and iodine status indicators: Child goiter was significantly correlated to Sequential (r=0.39, p=0.0011) but not to Simultaneous indices. Likewise child UIE was significantly correlated to Sequential (r=0.2, p=0.05) but not to Simultaneous indices. However no significant differences of cognitive test results were seen between children who had goiter versus those without. For mothers there was no significant difference based on the presence or absence of goiter for all the tests.

Relation between mother and child cognitive functions: Both Sequential (r=0.21, p= 0.03) and Simultaneous (r=0.29, p=0.004) indices were correlated for mothers and children. Mothers' education was also significantly correlated to children's Sequential as well as Simultaneous indices (r=0.19, p=0.04 and r=0.30, p=0.002, respectively) (Table 4.22). They shared a similar diet which might influence the cognitive development of both. The correlation might also reflect the mothers' ability to create stimulating environments. This indicates that the mothers and their children have similarities in cognitive function as evidenced by the results from this study.

DISCUSSION

The purpose of this study was to assess the iodine status and cognitive function of mother-child pairs in a rural village in Southern Ethiopia. The outcome of this study shows important demographic and socioeconomic characteristics of the subjects. The participant mothers' educational status was very low. Forty eight percent of the mothers

had no formal education. This lack of education may have a major effect on their knowledge regarding healthy food habits. The use of iodized salt in this community was very low with participants reporting only 2% use in the household. Similar results were reported in a nationwide study conducted in 2007 (5). Most of the households owned land and animals but the consumption of animal products as well as vegetables and fruits was also low. These results might be explained by lack of appropriate nutrition knowledge. Furthermore, the most frequently consumed vegetables were cabbage and kale which can contain goitrogens and which might contribute to lowering iodine status (15).

Stunting (height-for-age, <-2 Z-score) was high for children (29%) with underweight (weight-for-age, <-2 Z-score) at 12%. Moreover 14% of the mothers had BMIs that classified them as underweight. Anthropometric data obtained from this study show the presence of malnutrition among the mothers and children in the community.

The goiter check and grading were conducted by a physician from Hawassa University. Of the 68 mothers who came for the checkup, 85% had goiters ranging from grade I to IV and the children had 33% from grade I to III. The one mother with grade IV goiter was excluded from the study following the recruitment criteria. The high rate of occurrence and the severity of goiter was an indication of persistent, serious and long term iodine deficiency in the community. The high goiter rate was consistent with a recent nationwide study where the total goiter rate of children in the region was reported to be 56.2% and goiter rate of mothers to be 59.9 (5,6) Similarly the UIE results were very low. All UIE values were < 49 μg/L for both mothers and children, which is the upper cutoff point in the range for moderate iodine deficiency (20-49μg/L). Ninety nine percent of the mothers and 95% of the children had less than 20 μg/L UIE, the cutoff

point for severe iodine deficiency. Once again the results are consistent with results from previous studies where the mean UIE was found to be 30.1μg/L in the region (5). Significant correlation was observed between mothers' and children's UIE ($r = 0.29$, $p = .003$).

The range of cognitive test scores was very wide and the minimum scores for almost all tests were very low. The children's score was much less than mothers' in most tests. Both Sequential ($r=0.21$, $p= 0.03$) and Simultaneous ($r=0.29$, $p=0.004$) indices were significantly correlated for mother and children. We might say this shows similarities in cognitive function of the child and the mother. This might be attributed to consumption of similar diets. Similarities between mother and child might also be due to similar degree of environmental stimulation. Over all the cognitive test results for both the mothers and the children were low, especially for tests from Simultaneous and Planning indices (Triangles, Conceptual Thinking, Rover, Block Counting and Pattern Reasoning). This might be an indication of the subject's difficulty of being able to visualize, perceive, store and manipulate visual patterns. This might be due to physical consequences from iodine deficiency. There was significant relation between Z-scores and cognitive results specifically for height-for-age and weight-for-age. By analysis of variance, the more malnourished children (<-2 Z-score) performed significantly more poorly on the cognitive tests.

The fact that mothers' Raven's CPM score was predicted ($R^2 = 0.205$, $p<0.0001$) by BMI, latrine availability and mothers' education indicates that better nourishment, availability of a sanitary facility and education affected cognitive performance. Availability of a latrine also shows the subject's willingness to learn since latrine

building was introduced recently. In general the mothers' iodine status, as well as cognitive test results, was low indicating the significance of iodine for cognitive development.

Child goiter was significantly correlated to Sequential ($r=0.39$, $p=0.0011$) but not to Simultaneous indices. Likewise child UIE was significantly correlated to Sequential ($r=0.19$, $p=0.05$) but not to Simultaneous indices. The simultaneous processing requires the ability of reasoning and visualizing patterns. This result showed that the ability of visualization and thinking in visual pattern was more affected than sequential indices by iodine deficiency and malnutrition. Impaired cognitive development and visual processing as a result of iodine deficiency might contribute to the aforementioned results.

Results from this study show the existence of malnutrition in the community. In addition it is evidenced that the iodine status of both mothers and children was very low. The cognitive test results indicate a very poor cognitive performance as measured by both Raven's CPM and Kaufman ABC-II assessments.

Table 4.1. Subjects' characteristics

Variables	frequency (f)	Mean[1]	Ranges
Mothers' age (yr)	99	28.7 ± 5.6	17-45
Mothers' Ht (cm)	96	159.3± 5.8	147.8-170.5
Mothers' Wt (kg)	98	52.4 ± 6.8	39-77
Mothers' BMI (kg/m^2)	96	20.6 ± 2.4	15.2-29
Children's age (mo)	100	61 ± 3	54-72
Children's Ht (cm)	100	104 ± 6	89-121.1
Children's Wt (kg)	100	16.4 ±2.1	12.2-21.2
Family size	99	7 ± 3	3-16

[1] Mean ±SD

Table 4.2. Educational characteristics

Variables		Frequency (f)	Percentage (%)
Mothers' education	Illiterate	48	48
	Primary (1-4)	29	29
	5th grade & above	23	23
Household head	Wife	6	6
	Husband	92	92
	Grand parents	1	1
	Husband and wife	1	1
Household head's education	Illiterate	31	31
	Primary (1-4)	20	20
	5th grade & above	49	49

Table 4.3. Socioeconomic characteristics

Variables		Frequency (f) n=100	Percentage (%)
Animal owner ship	Yes	84	84.9
	No	15	15.1
Animals owned	Cow	75	75.8
	Goat	3	3.1
	Sheep	8	8.2
	Chicken	35	35.7
	Others	4	4.1
Land ownership	Yes	75	76.0
	No	24	24.0
Land size	500-1000 m^2	30	40.5
	1001-2000 m^2	11	14.8
	2001-3000 m^2	9	12.0
	>3001 m^2	24	32.4

Table 4.4. Housing conditions

Variable		Percentage (%) n=100
Window	Wooden	57
	No window	43
Roof	Grass (thatched)	67
	Iron sheet	33
Wall	Wood & mud	93
	Wood & grass	6
Latrine	Pit latrine	96
If Yes	Only pit	37
	Pit with house	57
	Improved pit latrine	1

Table 4.5.Water, health care and availability of other facilities

Variable		Percentage (%) n=100
Mosquito net		87
Water source		
	Tap[1]	78
	Protected well	20
	Unprotected well	1
Water treatment	Chlorine,	91
	Filter with cloth (for drinking only)	9
Iodized salt use	Yes	2
	No	98

[1]Tap = Public tap water treated with chlorine

Table 4.6. Children's Z-scores for anthropometric measurements (n=100)

Child Z Scores	<-3 Z-score (%)	≥ -3 to <-2 Z-score (%)	≥-2 Z-score (%)	>2 Z-score (%)
Ht-for-age[1]	10	19	71	0
Wt-for-age[2]	0	11	89	0
Ht-for-wt[3]	0	4	96	0

[1]For Ht-for-age: n= 29 for Z-scores< -2; n= 71 for Z-scores≥ -2
[2]For Wt-for-age: n= 11 for Z-scores< -2; n= 89 for Z-scores≥ -2
[3]For Ht-for-Wt: n= 4 for Z-scores< -2; n= 96 for Z-scores≥ -2

Table 4.7. Mothers' goiter grade and occurence[1]

Goiter grade	Frequency (f) (n=67)	Percentage (%)
0	10	14.9
I	17	25.3
II	27	40.3
III	13	19.4

[1] One mother with goiter grade IV was excluded from the study

Table 4.8. Children's goiter grade and occurrence

Goiter grade	Frequency (f) (n=67)	Percentage (%)
0	45	67.2
I	18	26.9
II	3	4.5
III	1	1.5

Table 4.9. Urinary iodine excretion values of mothers

UIE[1]	Percentage (%) (n=100)
<1 µg/L	71
1.1-10 µg/L	26
10.1- 20 µg/L	2
> 20 µg/L	1

[1]The median UIE for mothers was 1 µg/L

Table 4.10. Urinary iodine excretion values of children

UIE[1]	Percentage (%) (n=100)
<1µg/L	66
1.1-10µg/L	27
10.1- 20µg/L	2
> 20µg/L	5

[1]The median UIE for Children was 1 µg/L

Table 4.11. Mothers' cognitive test results

Variables	Frequency (f)	Mean[1]	Ranges	Max Scores[2]
Ravens CPM	100	19.87 ± 4.30	6-29	36
Pattern Reasoning[3]	100	5.36 ± 4.61	0-23	63
Block Counting[4]	100	7.70 ± 5.76	0-38	44
Number Recall[5]	100	8.74 ± 1.97	5-17	22
Rover[4]	99	15.52 ± 6.86	0-32	44
Word Order[5]	99	17.24 ± 5.70	8-30	31
Simultaneous[4]	99	23.28 ± 10.08	0-55	88
Sequential[5]	99	26.02 ± 6.34	13-41	53

[1]Mean ± SD
[2]Max score, the total maximum score for available particular test
[3] Planning
[4] Simultaneous
[5] Sequential

Table 4.12. Children's cognitive test results

Variables	Frequency (f)	Mean[1]	Ranges	Max Score[2]
Triangles[3]	98	5.08 ± 3.01	0-13	29
Pattern Reasoning[3]	97	2.0 ± 1.18	0-5	36
Conceptual thinking[3]	100	3.3 ± 3.15	0-13	28
Number recall[4]	100	5.23 ± 1.73	1-9	22
Hand Movement[4]	99	4.22 ± 2.14	0-11	23
Word Order[4]	99	8.64 ± 3.59	3-20	31
Simultaneous[3]	99	10.44 ± 5.31	1-25	93
Sequential[4]	99	18.12 ± 6.02	7-32	76

[1] Mean + SD
[2]Max score = the total maximum score for the particular test
[3] Simultaneous
[4] Sequential

Table 4.13. Effects of malnutrition on children's cognitive test results (Mean±SD)

	n	Tri[1]	CT[2]	PR[3]	WO[4]	NR[5]	HM[6]	Sequ[7]	Simul[8]
HAZ									
<-2	29	3.25 ± 2.39	2.13 ± 2.06	1.74 ± 1.12	7.17 ± 3.12	4.58 ± 1.78	3.03 ± 1.77	14.85 ± 5.49	7.15 ± 3.24
≥-2	71	5.77 ± 2.94	3.77 ± 3.39	2.10 ± 1.19	9.22 ± 3.62	5.49 ± 1.66	4.69 ± 2.10	19.40 ± 5.77	11.67 ± 5.42
P		0.0001	0.02	0.18	0.01	0.02	0.0004	0.0005	0.0001
WAZ									
<-2	11	2.11 ± 1.76	1.10 ± 1.19	1.75 ± 1.16	6.88 ± 2.57	4.00 ± 1.88	2.22 ± 1.30	13.22 ± 5.14	4.75 ± 2.49
≥-2	89	5.38 ± 2.95	3.54 ± 3.20	2.02 ± 1.18	8.82 ± 3.64	5.36 ± 1.67	4.42 ± 2.11	18.61 ± 5.91	10.96 ± 5.20
P		0.0016	0.0192	0.53	0.1246	0.0177	0.0029	0.009	0.001

[1]TR= Triangles
[2]CT= Conceptual Thinking
[3]PR= Pattern Reasoning
[4]WO= Word Order
[5]NR= Number Recall
[6]HM= Hand Movement
[7]Sequ=Sequential
[8]Simul = Simultaneous

Table 4.14. Comparison of children's cognitive tests by sex (Mean± SD)

Child Sex	Tri[1]	CT[2]	PR[3]	WO[4]	NR[5]	HM[6]	Sequ[7]	Simul[8]
Female	4.52 ± 2.79	3.07 ± 3.38	1.83 ± 1.0	8.19 ± 3.52	5.03 ± 1.82	3.94 ± 2.20	17.21 ± 6.01	9.53 ± 5.0
Male	5.68 ± 3.15	3.54 ± 2.89	2.16 ± 1.32	9.12 ± 3.64	5.43 ± 1.63	4.52 ± 2.06	19.08 ± 5.95	11.40± 5.51
P	0.06	0.46	0.17	0.20	0.25	0.18	0.12	0.08

Female; n=52
Male; n= 48
[1]TR= Triangles
[2]CT= Conceptual Thinking
[3]PR= Pattern Reasoning
[4]WO= Word Order
[5]NR= Number Recall
[6]HM= Hand Movement
[7]Sequ=Sequential
[8]Simul = Simultaneous

Table 4.15. Comparison of children's Z-score by sex

	Female n=52 (%)	Male n=48 (%)
HAZ [1]		
<-2	34.6	22.9
≥-2	65.4	77.1
Mean ± SD	-1.37 ± 0.17	-1.12 ± 1.34
WAZ[2]		
<-2	11.5	8.3
≥-2	88.5	91.7
Mean ± SD	-1.02 ± 0.14	-0.95 ± 0.80
WHZ[3]		
<-2	3.9	4.2
≥-2	96.1	95.8
Mean ± SD	-0.26 ± 0.12	-0.33 ± 0.82

[1]HAZ=Height-for-age
[2]WAZ=Weight-for-age
[3]WHZ=Weight-for-height

Table 4.16. Linear regression analysis predicting maternal Raven's CPM

	B	partial R^2	P
Intercept	15.06		<0.0001
M-Ed[1]	0.75	0.13	<0.0001
Latrine type	1.47	0.08	0.0023

Adjusted $R^2 = 0.19$, $R^2 = 0.21$
n = 99
[1]M-Ed = Mothers' education

Table 4.17. The effect of mothers' education on mothers' and children's cognitive test scores

	Level of Education		
	No Education[4]	1-4yrs[4]	≥5yrs[4]
Mothers			
Ravens CPM	18.83[b]	19.62[b]	22.34[a]
Pattern Reasoning[1]	3.33[c]	5.89[b]	8.91[a]
Block Counting[2]	6.33[b]	7.86[b]	10.34[a]
Rover[2]	13.0[c]	16.65[b]	19.26[a]
Number Recall[3]	7.97[a]	9.10[a]	9.86[a]
Word Order[3]	15.21[b]	18.58[a]	16.69[b]
Children			
Simultaneous[2]	9.28[b]	9.85[b]	13.63[a]
Sequential [3]	17.06[b]	18.27[b]	20.08[a]

[1] Planning
[2] Simultaneous
[3] Sequential
[4] Mean
P<0.05

Table 4.18. Linear regression analysis predicting child Simultaneous index results

	B	Partial R^2	P
Intercept	-19.71		0.04
HAZ[1]	10.19	0.23	< 0.0001
C-age[2]	0.41	0.07	0.004
M-Ed[3]	0.66	0.05	0.009
WHZ[4]	11.22	0.02	0.08
M-age[5]	0.16	0.03	0.05
WAZ[6]	-14.02	0.01	0.13

$R^2 = 0.42$
n = 89
[1]HAZ = Height-for-age
[2]C-age = Children's age
[3]M-Ed=Mothers' education
[4] WHA=Weight-for-height
[5]M-age = Mothers' age
[6]WAZ = Weight-for-age

Table 4.19. Linear regression analysis predicting child Sequential index results

	B	Partial R^2	P
Intercept	-16.20		0.14
HAZ[1]	1.78	0.15	<0.0001
C-Age[2]	0.57	0.09	0.001
Roof	3.01	0.03	<0.03
F-size[3]	-0.41	0.02	0.05

Adjusted $R^2 = 0.28$ $R^2 = 0.31$
n = 98
[1]HAZ = Height-for-age
[2]C-age = Children's age
[3]F-size=Family size

Table 4.20. Correlation matrix of mothers' results and the other study variables

	Ravens[1]	M-PR[2]	M-Simul[3]	M-Sequ[4]	M-Ed[5]	M-BMI[6]	HH-Ed.[7]	Roof	Window
Ravens[1]									
M-PR[2]	.40***								
M-Simul[3]	.45***	.37***							
M-Sequ[4]	.37***	.30***	.29**						
M-Ed[5]	.31**	.48***	.41***	.42***					
M-BMI[6]	.16	-.01	.03	.05	-.00				
HH-Ed.[7]	.24*	.27**	.20*	.27**	.55***	-.05			
Roof	.10	.13	-.03	.25**	.27**	.04	.22*		
Window	.07	.22	.10	.19	.28**	.21*	.20*	.57***	
Latrine	-.03	.13	.05	.03	.13	-.03	.10	.14	.13

[1]Ravens = Ravens Colored Progressive Matrix *P≤.05** P≤.01 ***p≤.001
[2]M-PR= Mothers' Pattern Reasoning
[3]M-Simul= Mothers' Simultaneous
[4]M-Sequ= Mothers' Sequential
[5]M-Ed= Mothers' education
[6]M-BMI=Mothers' body mass index
[7]HH-Ed= Household head educational status

Table 4.21. Correlation matrix of children's results and the other study variables

	C-UIE[1]	C-Sequ[2]	C-Simul[3]	C-age[4]	HAZ[5]	WAZ[6]	C-goiter[7]	HH-Ed.[8]	Latrine
C-UIE[1]									
C-Sequ[2]	.20*								
C-Simul[3]	.06	.50***							
C-age[4]	.08	.32***	.29**						
HAZ[5]	.12	.40***	.48***	.04					
WAZ[6]	.15	.39***	.48***	.06	.76***				
C-goiter[7]	.21	.39***	.13	.04	.16	.18			
HH-Ed[8]	-.08	.23*	.25**	-.01	.24**	.23**	.07		
Latrine	.08	.24**	.23*	.12	.14	.04	.06	.10	
Roof	.05	.22*	.05	.12	-.00	.06	0.28*	.22*	.14

[1]C-UIE= Children's urinary iodine excretion
[2]C-Sequ= Children's Sequential
[3]C-Simul= Children's Simultaneous
[4]C-age= Children's age
[5]HAZ=Height-for-age
[6]WAZ=Weight-for-age
[7]C-goiter=Child goiter
[8]HH-Ed= Household head educational status

*P≤.05 **P≤.01 ***P≤.001

Table 4.22. Correlation matrix of related mother-child variables

	m-UIE	BMI	M-Seq	M-Sim	M-Ed	M-PR	M-Wt	c-UIE	C-Seq	C-Sim	HAZ	WAZ
m-UIE[1]												
BMI[2]	.10											
M-Seq[3]	-.01	.05										
M-Sim[4]	.13	.03	.29**									
M-Ed[5]	-.04	-.00	.42***	.41***								
M-PR[6]	.01	-.01	.40***	.37***	.48***							
M-Wt[7]	.08	.83***	.17	.13	.08	.06						
c-UIE[9]	.30**	-.02	.21	.23*	.12	.08	.01					
C-Seq[10]	-.05	.23*	.21*	.09	.20*	.23*	.19*	.20*				
C-Sim[11]	.08	.20*	.16	.29**	.30**	.26**	.26**	.06	.50***			
HAZ[12]	.07	.05	.14	.08	.14	.11	.18	.12	.40***	.48***		
WAZ[13]	.01	.22*	.13	.11	.20*	.13	.29	.15	.39***	.48***	.76***	
WHZ[14]	-.07	.27**	.01	.06	.10	.05	.22	.08	.07	.11	-.12	.55***

[1]m-UIE= Maternal urinary iodine excretion
[2]BMI= Mothers' body mass index
[3]M-Seq= Mothers' Sequential
[4]M-Sim= Mothers' Simultaneous
[5]M-Ed.= Mothers' education
[6]M-PR= Mothers' Pattern Reasoning
[7]M-Wt= Mothers' weight
[8]M-Ht= Mothers' height
[9]c-UIE= Children's urinary iodine
[10]C-Seq= Children's Sequential
[11]C-Sim= Children's Simultaneous
[12]HAZ=Height-for-age
[13]WAZ=Weight-for-age
[14]WHZ=Weight-for-age
*P≤.05 **P≤.01 ***P≤.001

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CHAPTER V

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Summary of Findings

The purpose of this study was to assess the iodine status and cognitive function of mother-child pairs in Wondo Genet, a rural village in Southern Ethiopia. Iodine status was assessed based on goiter occurrence and UIE. There was very high goiter prevalence in mothers as well as children and the UIE was extremely low for both groups. The results from this study were also consistent with available data from the region where the study was conducted.

The cognitive function was assessed by Ravens CPM, and age appropriate tests from the Kaufman ABC-II assessment. Tests from the Kaufman ABC-II were Pattern Reasoning, Block Counting, Rover, Word Order, Number Recall, Hand Movement, Triangles and Conceptual Thinking. Though the cognitive test results were low in all cases, both mothers and children had more difficulty on tests making up the simultaneous and planning indices than the sequential index.

A household questionnaire was also administered to assess demographic and socio-economic characteristics, feeding patterns, and iodized salt use. The use of iodized salt was extremely low (only 2%) in the participants' households. Anthropometric measurements were also taken to assess long and short term malnutrition. The outcomes

of Z-scores for children and BMI for mothers indicated the presence of malnutrition among the study subjects. Malnutrition affected cognitive performance of children.

Testing of null Hypotheses

Ho1: The iodine status of mothers and their five-year children will be in the normal range. The iodine status of both the mothers and children was very low as measured by UIE and goiter. Therefore the null hypothesis one is rejected.

Ho 2: Iodine status has no effect on cognitive function of the subjects. The cognitive function was substantially below international norms. The subjects UIE was below 49μg/L and there was high occurrence of goiter for both mothers (85%) and children (33%). Because of this association the null hypothesis is rejected.

Ho 3: The cognitive function of the mother has no relation to their children. The result showed significant correlation of maternal cognitive test results with their five-year old children. Therefore the null hypothesis three is rejected.

Conclusions

Iodine deficiency continues to be the most common micronutrient deficiency and the single most preventable cause of mental retardation (1). Despite huge international efforts to eliminate iodine deficiency, it still remains a public health threat and IDD persists and continues to exist (5). Globally, in the year 2006, 54 countries remained with problems of iodine deficiency.

Salt iodization is believed to be the most cost-effective method to combat iodine deficiency. The distribution of iodized salt costs 5-10 US cents per year per individual (23, 38) . The countries left behind are the poorest countries with few or no laboratory facilities and limited technical skill to properly monitor salt quality in the iodization process (23). Ethiopia is one of these countries with only 20% access of households to iodized salt (12). Despite the fact that the daily recommended allowance of iodine for adult is only 150μg its bioavailability is dependent on iodine content of the diet.

Bioavailability of iodine can also be reduced by certain plant foods containing goitrogens. Cabbage and kale are among the frequently consumed food items in the study area that could have been sources of goitrogens. Furthermore, only two households (2%) used iodized salt and 91% never consumed fish.

The high prevalence of goiter and the low urinary iodine excretion demonstrate serious long and short-term iodine deficiency in the study area. Low scores in cognitive test performance might be attributed to iodine deficiency and its consequences. In conclusion, there was a strong indication that the study participants were severely iodine deficient. The results also show the existence of malnutrition. Other nutrients might also be deficient as evidenced by the correlation of stunting and cognitive test scores.

Efficient and cost effective methods to secure iodine availability in the community are urgently needed. The problem of food security should also be addressed to improve the nutritional status in the area.

Recommendations

It was evident from this study that women and children from the study area were seriously suffering from iodine deficiency. It was also evident that brain development of the children is at stake since iodine deficiency immensely affects brain development and cognitive function (4).

Immediate attention must be given and adequate budget should be allocated to eradicate the problem. Political will and strong law enforcement are required from the government. Iodized salt should be made available at affordable prices, and a monitoring mechanism should be set to control the distribution of iodized salt for human consumption. Target-oriented campaigns should be launched to create awareness for salt producers as well as consumers. Iodine supplementation and food fortification options should also be considered. More research is needed to follow progress and to plan more appropriate interventions with special emphasis on women of childbearing age and young children.

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APPENDICES

APPENDIX A

Questionnaire (English)

ሓዋሳ ዩንቨርሲቲ
Hawassa University
አዋሳ ግብርና ኮሌጅ
Awassa College of Agriculture

Maternal and child iodine status study questionnaire

The purpose of this questionnaire is to identify factors affecting iodine.
Status in women of childbearing age and their five-year-old children, It will help to propose solutions to possible problems based on the findings.
For this reason, your response will greatly help us in fulfilling the goal of the study. Once again we assure you the information you have given us will be used for the study purpose exclusively.

Thank you

Name of the mother _____
Name of the child_____

Demographic and socioeconomic information

1. Regional state SNNRS 2.Zone Sidama
3. District Wondo genet
4. Kebele / county Gotu onoma
5. Interview date ____M____D_____Y
6. Interviewers Name_____
7. Time the interview began _____
8. Time the interview ended_____
9. Mother's ID_____
10. Birthdate (mother) ___M____D_____
11. Mother's age_____
    If mother's age is approximation what did you use? _____
12. Child's ID_____
13. Birthdate (child) __M__ D___Y 14. Age of child_____
    Did you use immunization card to see the age of the child Yes_____No_____
15. The child's Sex_____

No	**question**	**Id**
01	Number of people in your household	Children average 7.2 _____ Others
02	What is your religion?	1. Orthodox Christian 12% 2. Protestant Christian 85% 3. Catholic 1% 4. Muslim 1% 5. Any other (explain)_____ 1%
03	Marital status of the mother	1. Married 92% 2. Never married - 3. Separated 2% 4. Widowed 6% 5.Divorced -
04	How many years of schooling did the respondent (the mother) complete?	1. None 48% 2. First grade 4% 3. Second grade 7% 4. Third grade 8% 5. Fourth grade 10% 6. Fifth grade and above 23%
05	Who is the head of the household?	1. The mother (the respondent) 6% 2. The father (husband) 92% 3. Grandparent (mother or father) 1% 4.Uncle or aunt - 5. Other (specify) -

06	Educational status of the head of the household	1. Illiterate 31% 2. First grade - 3. Second grade 4% 4. Third grade 5% 5. Fourth grade 11% 6. Fifth grade and above 49%
07	Do you own land?	Yes 76% No 24% 1 2 If yes how much? _____ hectare
08	What is the main occupation of head of household?	1. Private farm 48% 2. Tenant (working to share with a land owner) 4% 3. Farm laborer 4% 4. Daily laborer 14% 5. Self employed (other than farming) 7% 6. Employee (other than farm) 2% 7.Unemployed (not working) - 8. Other (specify) two or more of the above 18%
09	Do you have any livestock?	1.Yes 85% 2. No 15%
10	If Yes what and how much?	1. Cows and oxen (number)_____76% 2. Goats (number)_____ 3% 3. Sheep (number)_____ 8% 4. Poultry (number)_____ 36% 5. Others (number)_____ 4%
11	What is the main source of the household drinking water?	1. Tap water (public tap) 79% 2. From protected well or spring 20% 3. From unprotected well or spring 1% 4. From a river - 5. From a lake or dam -
12	Do you treat the drinking water?	Yes 84% (pre-treated tap water) No 14%
13	If yes, what do you use to treat?	1.Chlorine 91% (tap-water) 2. Boiling - 3. Filter using cloth (cloth as a filter) 4% 4. Other (specify) 6%
14	How far is the water source from your house?	Hrs walk_____ Meter/ km_____

15	What type of toilet facility does your household use?	1. Pit latrine 2.Pit latrine with sides/walls 3 Ventilated improved pit latrine 4.Flush toilet 5.We don't have toilet	37% 56% 1% - 4%
16	What are the walls of your house made of?	1. From wood and mud 2. From dry mud blocks 3. From wood and grass 4. From concrete 5. Other (specify)	94% 6% - - -
17	What is the roof of your house made of?	1.Made of grass/straw/reed thatch 2.Corrugated iron sheet 3. Other (specify)	67% 33% -
18	What are the windows of your house made of?	1.I don't have a window 2.Open window (no pane) 3. Made of (net) mesh 4.Glass 5.Wooden pane(shutter) 6.Other (specify)	43% - - - 56% 1%
19	Where does the household go for medication?	1.Clinic or health center 2. Traditional medication 3. Religious healing (prayer) 4. Other (specify)	100% - - -
20	Do you use mosquito net at night?	1. Yes 2. No	87% 3%
21	What kind of salt do you use?(please list the places they usually buy salt)	1.Iodized 2.Un-iodized	2% 98%
22	Among the following how often are these foods in your diet?	Daily Per 3 days wk 15 days 1month Never 1y 1 % 2 % 3% 4 % 5 % 6% 7%	
	your usual diets?	33 22 33 5 6 1 -	
	1. _____ Vegetables	18 21 31 10 17 2 1	
	2._____Fruits	14 19 30 11 17 8 1	
	3. _____Legumes	76 7 5 2 8 11 -	
	4 _____ Cereals and grains	39 25 15 4 16 1 -	
	5. _____ Roots and tubers	- 2 19 9 35 15 20	
	6. _____ Egg	- - 1 1 30 17 30	
	7. _____ Chicken	- - 4 10 28 6 47	
	8 _____Beef/mutton	- - 1 - 3 92 4	
	9. _____Fish	30 12 13 6 6 30 3	
	10. _____Whole milk	22 9 23 7 12 23 3	
	11._____ Skimmed milk	4 3 17 12 23 41 3	
	12._____ Cottage cheese	7 5 4 2 12 68 2	

	13_____Whey	1	-	2	2	6	88	1
	14 _____Oil seeds	97	3	-	-	-	-	-
	15. _____Oil	7	10	15	7	34	13	14
	16. _____Butter							

Mother and child anthropometric measures

ID	Weight measurements			Mean (std)	Height measurements			Mean(std)
	1st	2nd	3rd		1st	2nd	3rd	
Mothers'				52.66±6.3				159.85±6.16
Child's				16.86±1.86				105.4±6.62

APPENDIX B

Questionnaire (Amahric)

ሓዋሳ ዩንቨርሲቲ
Hawassa University
አዋሳ ግብርና ኮሌጅ
Awassa College of Agriculture

የእናቶችና የልጆቻቸው አዮዲን መጠን ጥናት የተዘጋጀ መጠይቅ

ይህ መጠይቅ የተዘጋጀው የእናቶችና የ5አመት ልጆቻቸው አዮዲን መጠን ሁኔታንለማጥናትና ለሚገኙ ችግሮችም የመፍትሔ ሀሳቦችን ለመጠቆም ታስቦ ነው።። ስለዚህም እርስዎ ለመጠይቆቹ አግባብነት ያለው ምላሽ በመስጠት የሚያደርጉት ትብብር የጥናቱን ዓላማ ለማሳካት ከፍተኛ ድርሻ አለው።። በተጨማሪም ማንኛውም ዓይነት የግል መረጃዎ ለጥናቱ ብቻ ተወስኖ እንደሚቀር ልናረጋግጥልዎ እንወዳለን።።

እናመሰግናለን

በሲዳማ ዞን የእናቶችና የልጆች የአዮዲን መጠንና የአእምሮ አድገት ጥናት የተዘጋጀ መጠይቅ

የእናቲቱ ስም_____ ልጁ/ቷ ስም_____

የቤተሰብና ማህበራዊ ሁኔታ መረጃ መጠየቂያ ቅጽ

ክልል_____ዞን_____ወረዳ_____ቀበሌ መስተዳድሩ ስም_____
ቃለ መጠይቅ የተደረገበት____ወር____ቀን____ዓ ም የጠያቂው ስም_____
ቃለመጠይቁ የተጀመረበት ሰዓት_____ ያለቀበት ሰዓት_____
የእናቲቱ መለያ ቁጥር_____እናቲቱ የልደት____ወር_____ ቀን_____ዓ ም
የእናቲቱ ዕድሜ_____የእናቲቱ ዕድሜ በግምት ከሆነ እንዴት ገመቱ?_____
የልጁ/ቷ መለያ ቁጥር ___የልጁ/ቷ የልደት_____ወር__ቀን____ዓ ም
የልጁ/ቷ ዕድሜ_____
የልጁ/ቷን ዕድሜ ለመገመት የክትባት ካርድ ተጠቅመዋል?
አዎን_____አልተጠቀምኩም_____የልጁ/ቷያታ_____

ቁጥር	ጥያቄዎች	መለያ
01	የቤተሰብዎ ብዛት ስንት ነው?	_____ልጆች _____ሌሎች
02	ሀየማኖትዎ ምንድ ነው?	1.ኦርቶዶክስ 2.ፕሮቴስታንት 3.ካቶሊክ 4.ሙስሊም 5.ሌላ ከሆነ ይግለፁ _____
03	የእናቲቱ የጋብቻ ሁኔታ	1.ገባች 2.ያላገባች 3.የተለያየች 4.ባል የሞተባት 5.የፈታች
04	ተጠያቂዋ(እናት) ስንተኛ ክፍል ድረስ ተምረዋል?	1.ያልተማረ 2.አንደኛ ክፍል 3.ሁለተኛ ክፍል 4.ሶስተኛ ክፍል 5.አራተኛ ክፍል 6.አምስተኛ ወይም ከዚያ በላይ
05	የቤተሰቡ አስተዳዳሪ ማን ነው?	1.እናት(ተጠያቂዋ) 2.ባል(አባት) 3.አያት(ሴት/ወንድ) 4.አክስት/አጎት 5.ሌላ ከሆነ ይግለፁ

06	የቤተሰቡ አስተዳዳሪ የትምህርት ደረጃ	1.ያልተማረ 2.አንደኛ ክፍል 3.ሁለተኛ ክፍል 4.ሶስተኛ ክፍል 5.አራተኛ ክፍል 6.አምስተኛ ወይም ከዚያ በላይ
07	ይመሬት ይዞታ አለዎት?	አዎን የለኝም 1 2 ካለዎት ምንያህል? _____ሄክታር
08	የቤተሰቡ አስተዳዳሪ መተዳደሪያ ምንድ ነው?	1.የግል እርሻ 2.ጭሰኛ(የጋራ የሚያርስ) 3.እርሻ ላይ ተቀጥሮ የሚሰራ 4.የቀን ሰራተኛ (ከእርሻ ውጭ) 5.የግል ተዳዳሪ(ከእርሻ ውጭ) 6.ተቀጣሪ ሰራተኛ(ከእርሻ ውጭ) 7.ስራ የሌለው(ተቀጣሪ ያልሆነ) 8.ሌላ ከሆነ ይግለፁ
09	ከብቶች አሉዋችሁ?	1.አዎን 2.የለንም
10	አዎን ከሆነ ምን ያህል ከብቶች አሉዋችሁ?	1.ላሞች በቁጥር _____ 2.ፍየሎች በቁጥር _____ 3.በጎች በቁጥር _____ 4.ዶሮዎች በቁጥር _____ 5.ሌላ በቁጥር _____
11	የቤተሰቡ ዋነኛ የመጠጥ ውሃ ምንጭ ምንድ ነው?	1.ከቧንቧ ወይም ከቦኖ 2.ከተከለለ ጉድጓድ ወምም ምንጭ 3.ከልተከለለ ጉድጓድ ወምም ምንጭ 4.ከወንዝ 5.ከሀይቅ ወይም ከግድብ
12	ለመጠጥ ምትጠቀሙት ውሃ የተጣራ ነው?	አዎን አይደለም
13	አዎን ከሆነ በምን?	1.በክሎሪን 2.አፍልተን 3. በጨርቅ አጣርተን 4.ሌላ ከሆነ ይግለፁ
14	በአማካይ ውሃ ከሚያገኙበት እስከ ቤትዎ ምን ያህል ይርቃል?	_____ሰዓት መንገድ _____ሜትር/_ኪ. ሜ

15	ቤተሰቡ የሚጠቀምበት የሽንት ቤት አይነት ምንድ ነው?	1.የደረቅ ጉድጓድ ሽንት ቤት 2.ዙሪያው የተከለለ ሽንት ቤት 3.የተሻሻለ ንፋሽ መግቢያ ያለው ሽንት ቤት(ቪ አይ ፒ) 4. በውሃ የሚሰራ ሽንት ቤት 5. ሽንት ቤት የለንም
16	የቤትዎ ግድግዳ የተሰራው ከምንድ ነው?	1.ከጭቃና እንጨት 2.ከደረቀ የጭቃ ጡብ 3.ከ እንጨትና ሳር 4. ከብሎኬት/ ግንብ 5.ሌላ ከሆነ ይግለፁ
17	የቤትዎ ጣራ የተሰራው ከምንድ ነው?	1.በሳር ከዳን 2.በቆርቆሮ 3.ሌላ ከሆነ ይግለፁ
18	የቤትዎ መስኮት የተሰራው ከምንድ ነው?	1.ቤቱ መስኮት የለውም 2.ክፍት መስኮት ነው(መዝጊያ የሌለው) 3.በመከለያ(ወንፊት) 4.በመስታወት 5.በእንጨት መዝጊያ 6.ሌላ ከሆነ ይግለፁ
19	ቤተሰቡ ህክምና የሚያገኘው ከየት ነው?	1.ከዘመናዊ የህክምና መስጫ (ክሊኒክ) 2.ከባህል ህኪም 3.በኃይማኖታዊ ፈውስ(በፀሎት) 4.ሌላ ከሆነ ይግለፁ
20	የወባ መከላከያ አጎበር ትጠቀማላችሁ?	1.አዎን 2.አንጠቀምም
21	ለቤትዎ የሚቀጠሙት ምን ዓይነት ጨው ነው? (ተገዛበትን ቦታ ይመዝግቡ)	1.አዮዲን ያለበት 2.አዮዲን የሌለበት
22	ከሚከተሉት ውስጥ ቤተሰብዎ በአብዛኛወን ጊዜ የሚመገበው ምግብ ምንድ ነው? 1. አትክልቶች _____ 2.ራፍሬ _____ 3.ጥራጥሬ _____ 4.የአገዳ አህሎች_____ 5.ስራስሮች _____ 6.ንቁላል _____ 7.ዶሮ _____ 8.ስጋ _____ 9.አሳ _____ 10.ትኩስ ወተት _____	በየቀኑ=1 በ3ቀን=2 በሳምንት=3 በ15ቀን=4 በወር=5 ፍጹም =6

	11.አሬራ _____ 12.ኤይብ _____ 13.አጓት _____ 14.የቅባት እህሎች _____ 15.ዘይት _____ 16.ቅቤ _____	

የእናቶችና ልጁ/ቷ የሰውነት መጠነ ልኬት

መለያ ቁጥር	ክብደት			ቁመት			የ የክንድ መጠን ዙሪያ
	1ኛ ምልከታ	2ኛ ምልከታ	3ኛ ምልከታ	1ኛ ምልከታ	2ኛ ምልከታ	3ኛ ምልከታ	
እናት							
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APPENDIX C

Oklahoma State University Institutional Review Board (IRB) Approval

Oklahoma State University Institutional Review Board

Date:	Tuesday, February 06, 2007
IRB Application No	HE06105
Proposal Title:	Effects of Iodine Supplementation on Cognition in Iodine-Deficient Women of Child-Bearing Age and Their Five-Year-Old Children in Southern Ethiopia
Reviewed and Processed as:	Full Board

Status Recommended by Reviewer(s): Approved Protocol Expires: 11/7/2007

Principal Investigator(s ✓)

Alemtsehay Bogale Wotango	Yewelsew Abebe	Barbara Stoecker
40-8 S. Univ. Place	co-pi with D. Thomas	421 HES
Stillwater, OK 74075	Stillwater, OK 74078	Stillwater, OK 74078

The IRB application referenced above has been approved. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

☒ The final versions of any printed recruitment, consent and assent documents bearing the IRB approval stamp are attached to this letter. These are the versions that must be used during the study.

As Principal Investigator, it is your responsibility to do the following:

1. Conduct this study exactly as it has been approved. Any modifications to the research protocol must be submitted with the appropriate signatures for IRB approval.
2. Submit a request for continuation if the study extends beyond the approval period of one calendar year. This continuation must receive IRB review and approval before the research can continue.
3. Report any adverse events to the IRB Chair promptly. Adverse events are those which are unanticipated and impact the subjects during the course of this research; and
4. Notify the IRB office in writing when your research project is complete.

Please note that approved protocols are subject to monitoring by the IRB and that the IRB office has the authority to inspect research records associated with this protocol at any time. If you have questions about the IRB procedures or need any assistance from the Board, please contact Beth McTernan in 219 Cordell North (phone: 405-744-5700, beth.mcternan@okstate.edu).

Sincerely,

Sue C Jacobs

Sue C. Jacobs, Chair
Institutional Review Board

Oklahoma State University Institutional Review Board

Date	Tuesday, October 09, 2007	Protocol Expires:	10/8/2008
IRB Application No:	HE06105		
Proposal Title:	Effects of Iodine Supplementation on Cognition in Iodine-Deficient Women of Child-Bearing Age and Their Five-Year-Old Children in Southern Ethiopia		
Reviewed and Processed as:	Full Board **Continuation**		
Status Recommended by Reviewer(s)	**Approved**		

Principal Investigator(s)

Alemtsehay Bogale Wotango
40-8 S. Univ. Place
Stillwater, OK 74075

Yewelsew Abebe
co-pi with D. Thomas
Stillwater, OK 74078

Barbara Stoecker
421 HES
Stillwater, OK 74078

Approvals are valid for one calendar year, after which time a request for continuation must be submitted. Any modifications to the research project approved by the IRB must be submitted for approval with the advisor's signature. The IRB office MUST be notified in writing when a project is complete. Approved projects are subject to monitoring by the IRB. Expedited and exempt projects may be reviewed by the full Institutional Review Board.

☒ The final versions of any printed recruitment, consent and assent documents bearing the IRB approval stamp are attached to this letter. These are the versions that must be used during the study.

The reviewer(s) had these comments:

The protocol is approved for continued data analysis only. Any additional data collection must be submitted as a modification request for review and approval prior to its initiation.

Signature :

Sue C. Jacobs, Chair, Institutional Review Board

Tuesday, October 09, 2007
Date

APPENDIX D

Hawssa University Office of Vice President for Research and Extension Approval

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Tel. +046 220 47 38
220 96 76/77/78
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Hawassa University
Office of Associate Vice President for Research and Extension

P.O.Box 5, Awassa, ETHIOPIA
Fax: +046 2 20 65 17
E-Mail: atolera@yahoo.com

Ref:. H-VP/13/5140/99
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Date: 5/ 02/2007
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To: Oklahoma State University
Institutional Review Board

Subject: Approval of research proposal entited ''Effects of Iodine Supplementation on Cognition in Iodine-Deficient Women of Child-bearing Age and Their Five-year-old Children in Southern Ethiopia''

This is to inform that the Research Ethics Committee of Hawassa University has examined approved the procedures of the above mentioned proposal, and that the research can be executed starting from now.

The Federal Democratic Republic of Ethiopia
Hawassa University

With regards

Adugna Tolera (Ph D)
Associate Vice President for
Research and Extension

APPENDIX E

Script read to the subjects

Recruitment Script

Scientists from Hawassa University and the United States need your help. We want to know what makes women and children in your area healthy and smart. We are especially interested in iodine, which is an important part of the food we eat, and how it may affect our cognition. We are conducting a study for mothers and their five-year-old child. We are asking 100 women of childbearing age and their five-year-old child (100) from villages in Sidama to be in this study.

Procedures: If you agree to take part in this study we will ask your help in the following ways:

- Come to a central place in the village. First we will ask you some questions about your home such as who lives there and what kind of work they do. We will also ask what kinds of food you feed to your family. We will then measure yours' and your child's weight and height. We will also test you and your child on few cognitive tests. We will collect blood and urine from you and your child. We are collecting this blood to see how much iodine you and your child have. The blood collection will take only few minutes.
- All of these things will take one and half to two hour.

Risks and Benefits:

- The blood collection is a standard medical procedure that may cause momentary pain to you or your child, but you will hold him/her during this and will be able to comfort him/her. If the place where we took the blood does become sore or infected, either on you or your child please take your baby to your community health worker. He/she will put medicine on the sore and a bandage. If more medical attention is needed, the community health worker will help you get to the local health clinic where you or your child will be treated without cost to your family.
- If you or your child feels uncomfortable during the cognitive test you can take a break and comfort your child.
- We will examine yours' and your child's blood and urine to see if there is enough iodine in it. If there is not, we will notify you so that you can talk to the village community workers and health centers about what to do.
- Along with knowing if you and yours' child's blood and urine has enough iodine in it, we will also give you a photograph of you and your child and an article like a head kerchief and soap for you and a T-shirt and a short for him/her.
- There is no cost to you for being in this study.
- From this study, we hope to better understand how the types of food that your family eat affects the way your brain grow and develop.

Confidentiality: No one except those of us conducting this study will see the results of you and your child's blood and urine test, or your answers to the questions that we ask you or the results of the cognitive test. We will store these records in a locked office at Hawassa University and at a university in the United States. If any information about you

and your child is ever presented to other scientists at a meeting or in a written articles, neither your name nor your child's name will be identified.

Even if you agree for you and your child to be in this study, you may choose to quit at any time without any penalty. If you have questions after the testing has been done, you may contact your community health worker who will help you contact us so that we can answer them for you.

Thank you so much for your time and cooperation

APPENIDIX F

Consent Form

Consent Form

(To be read to participants in their own language after the information in the Script has been read)

Invitation for Questions:

You may ask any questions you have now about the study. If you have any questions later, you may ask your community health worker who will help you get your questions answered by contacting the people conducting this project. (The following contact information will be given to the community health worker. For general questions about the study: Dr. Yewelsew Abebe at Hawassa University, P.O. Box 5, Awassa or at, phone 046-206698. For questions regarding ethical standards: Dr. Adugna Tolera at the Hawassa University Ethics Committee at the Research and Extension Office at P.O. Box 5, Awassa, Phone 046-200221.)

I have been asked to take part in a research study that measures the amount of iodine in me and my five-year-old child's blood and urine and how that might relate to our cognition. We will also be tested on cognitive tests. The translator has told me the following things about the study

- That the study is being done to measure the iodine status of me and my five-year-old child, which is an important part of the food we eat, and how it may affect our cognition.
- That I will be asked several questions about my household the food we eat, and the way we live.
- That the main part of the study is to see how my child and I will and respond to different cognitive tests.
- That my child and I will be weighed and measured.
- That a small amount (~ 5ml) of blood will be taken from my child and me.
- That urine will be collected from my child and me.
- That my child may fuss during the activities, but that I will be there to comfort him/her.

- That all of this will take one and half to two hours.
- That there are possible risks discomforts, but also benefits of the study.
- That the information will be kept private.
- That I can receive free medical care from the community health worker if my child and I get hurt the study.
- That participating will cost me nothing and that I will receive a picture of me and my child. We will also receive a head kerchief and soap for me and a T-shirt and a short for him/her.
- That my child and I can stop being in the study at any time.
- That my child and I may be asked to be in other studies later.
- That I have been given the chance to ask questions about this study and our participation in it.
- That I can contact the community health worker if I have further questions.

Consent:

Agreeing to be in this study means that the research project has been described to me orally in language I understand. I have had a chance to ask questions about the study. These questions have been answered to my satisfaction before I have agreed for myself and my child to be in the study. I may choose for my child and me not to be in the study or I may quit being in the study at any time without loss of any privileges to which we are entitled. I know what will be done to me and to my child as part of this study. I also know the possible good and bad things (benefits and risks) that could happen if we are in this study. I choose for my child and me to be in this study. I know that I can stop being in this study at any time and we will still get the usual medical care.

I agree for my child and me to be in this study as described above.

Name of Participant (spoken to tape)_____

Name of Witness (spoken to tape)_____

Name of Translator (spoken to tape)_____

Date (spoken to tape)_____

VITA

Alemtsehay Bogale Wotango

Candidate for the Degree of

Master of Science

Thesis: IODINE STATUS AND COGNITIVE FUNCTION OF MOTHER-CHILD PAIRS IN SIDAMA, SOUTHERN ETHIOPIA

Major Field: Nutritional Sciences

Biographical:

Personal data: Born in Ethiopia, Addis Ababa in 1970.

Education: Graduated from Kotebe College of Teachers Education in 1998, received Bachelor of Science degree in Rural Development and Family Sciences from Hawassa University (then Debub University) in July, 2005; completed the requirements for the Master of Science in Nutritional Sciences at Oklahoma State University, Stillwater, Oklahoma in July, 2008.

Experience: Graduate Research Assistant at OSU (January 2006 to July 2008), served as Graduate Assistant at Debub University, Faculty of Agriculture, Department of Rural Development and Family Sciences (July 2005-December 30, 2005), served as a Technical Assistant at Debub University, Faculty of Agriculture, Department of Rural Development and Family Sciences (Nov.2001-June 2005), worked as a junior class teacher of Home Economics in different schools in the southern region (1992-June, 2001).

Professional Memberships: American Society for Nutritional Sciences

Name: Alemtsehay Bogale Wotango Date of Degree: July, 2008

Institution: Oklahoma State University Location: Stillwater, Oklahoma

Title of Study: IODINE STATUS AND COGNITIVE FUNCTION OF MOTHER-CHILD PAIRS IN SIDAMA, SOUTHERN ETHIOPIA

Pages in Study: 124 Candidate for the Degree of Master of Science

Major Field: Nutritional Sciences

Scope and Method of Study: Iodine deficiency affects brain development. The purpose of this study was to assess the iodine status and cognitive function of women of childbearing age and their five-year-old children. A total of 100 women and their five-year-old children participated in this cross-sectional study. Demographic and socioeconomic characteristics, dietary patterns including iodized salt consumption, anthropometric measurements, cognitive tests, goiter grading and urinary iodine excretion (UIE) were analyzed. Descriptive statistics, correlations and analysis of variance were calculated.

Findings and Conclusions: The use of iodized salt was only 2%. The study participants consumed very low amounts of animal source food. Stunting was 29% and mothers with BMI < 18.5 were 14%. Eighty five percent of the mothers and 33% of children had goiter ranging from grade I to III. All the participants had UIE concentration less than 49μg/L. Ninety nine percent of the mothers and 95% of the children had UIE concentration less than 20μg/L. The results of cognitive tests for both mothers and children were low especially for tests from Simultaneous and Planning indices. This might be an indication of the subjects' difficulty in being able to visualize, perceive, store and manipulate visual patterns which might be a consequence of iodine deficiency. Mean cognitive test scores for children were significantly affected by malnutrition (Z-scores <-2). In conclusion the study result strongly indicates that the study participants were severely iodine deficient and performed poorly in the cognitive tests.

ADVISER'S APPROVAL: Barbara J. Stoecker