DIETARY AND WATER RELATED FACTORS ASSOCIATED WITH ENDEMIC GOITRE IN SCHOOL CHILDREN IN AWASA DISTRICT, SOUTHERN ETHIOPIA.

BY

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DECLARATION

I, BERHANU HAILEGIORGIS hereby declare that this thesis is my original work and has not been presented for a degree in any other University.

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DEDICATION

This work is dedicated to my late parents Gete Mulugeta and Hailegiorgis Jemaneh.

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ABSTRACT

A case control study was carried out to identify factors associated with endemic goitre in school children, 6 - 18 years of age, in Awasa district in Sidamo region, South Ethiopia. The factors considered in the study were iodine intake, treated water supply, unprotected water supply, dietary pattern, nutritional status and fluorosis.

The cases (children with visible goitre) and controls (non-goitrous children) were individually matched for age and sex. A total of 235 individually matched case-control pairs were identified and studied. The investigation involved clinical examination of goitre and fluorosis, laboratory analysis of iodine in urine, anthropometric measurement and administration of a questionnaire.

The prevalence of goitre in school children in the study area was 61.7% out of which 11.7% was the visible goitre. The mean urinary iodine concentrations in both the case and control groups were 16.2 µg/dl with standard deviations of 9.7 and 9.9, respectively. This indicated that the iodine intake of the two groups was similar. Daily consumption of teff (Eragrositis abyissinica) was highly ($P<.0001$) associated with the presence of visible goitre in the study children. The odds ratio was 12.5.

High rate of consumption of sugarcane was also significantly (P<.001) associated with the occurrence of endemic goitre. A significant (P<.0001) association was observed between chlorinated water supply and the presence of visible goitre in the study children with an odds ratio of 5.3.

The results of this investigation suggest that daily consumption of teff, was the most important factor associated with the presence of visible goitre in the school children. Other factors found to have significant association include use of treated water supply and a high rate of sugarcane consumption. Since the iodine intake was similar in both groups, the results are therefore, further evidence that there are other important factors that could be associated with the occurrence of goitre, especially in the study area.

CHAPTER ONE

INTRODUCTION

1.1 Statement of the Problem

Goitre is known to be an ancient scourge of mankind (Hetzel, 1989). The first records of goitre date back to the ancient civilizations of the Chinese and Hindu cultures and then to Greece and Rome.

Endemic goitre is associated with a wide spectrum of physical and intellectual disorders which have far reaching health, economic and social consequences (Hetzel, 1987; Hershman, 1986; Levin, 1987). These disorders include: endemic cretinism (characterized most commonly by mental deficiency, deaf-mutism and spastic diplegia and neurological defects); impaired mental function in children and adults (associated with reduced levels of circulating thyroxine); and increased still births, perinatal and infant mortality. Thyroid carcinoma is also thought to occur more frequently in populations with endemic goitre (Wahner, 1956). Recent evidence indicates that more than 800 million people in Asia, Africa and South America are at risk of goitre and its associated anomalies.

That goitre is a problem of public health significance in

Ethiopia is no longer a matter of debate. Low iodine intake has been implicated to be the sole factor in the etiopathogenesis of endemic goitre in the country. There is however, a speculation by the people in the endemic areas that goitre and its associated disorders are probably the results of factors other than iodine deficiency (ENI, 1980). To date, there is no empirical evidence to substantiate the speculation. In some countries, implementation of iodine prophylaxis programmes has met considerable difficulties due to lack of knowledge concerning the causative factors of endemic goitre (Gaitan, 1980). Thus, it is quite apparent that investigating the factors associated with endemic goitre is a task of far-reaching practical importance, if goitre and its complications are to be eradicated.

1.2 Background

Goitre has been recognized as a medical problem in Ethiopia since the turn of the century (Kelly and Snedden, 1960). Travellers in Ethiopia between 1903 and 1904 reported high prevalence of goitre in the western part of the country, i.e., southern Tigray, Wollo, Wollega, Gojam and Shoa regions.

As part of the first nutrition survey conducted by Interdepertmental Committee on Nutrition for National Defence (ICNND) in 1959, goitre prevalence was reported to be between 4.4% and 12.5% in three areas where detailed examinations were made. In a survey which was carried out by United States Aid for International Development (USAID) in 1965, a goitre rate of 20% in males and 42% in females was found in Tigray province. Popov (1967), has also reported that in the remote villages of the mountainous Wollo region, between 10% - 28% of the population have visible goitre. Popov has also mentioned that 16% of all major operations performed at a hospital in the region are for goitre.

In another mountainous region, Gonder, in 750 persons examined goitre was found to have a peak prevalence (46.7%) in males in the age group 10-14 years (Molineax, 1967). In females in the same age group, the prevalence was 56.7% and the peak (90.2%) was reached in the group 30 - 39 years of age. The prevalence of goitre has also been studied in Addis Ababa and at two small towns to the west of the city (Hofvander, 1970). In this study, the prevalence was reported to be 8.5, 26.5, 53.0% in Addis Ababa and in the towns of Ijaji and Bako respectively. In all the three locations goitre rate increased with increasing age.

Hospital and health centre data from all over the country compiled by the Ethiopian Nutrition Institute (ENI) indicats that 12 out of the 14 regions had some pockets of endemic goitre (ENI, 1978). Based on this information, four areas in four regions from the northern, central, western and southern parts of Ethiopia were surveyed by the same institute. The results showed that overall prevalence of goitre was 53.6% out of which 27.7% was visible goitre. In the four areas surveyed, the incidence of goitre is found to be two to three times more in females than in males. Following this study the ENI conducted sample surveys at a national level on 35,635 school children and 19,128 general household members (ENI, 1983). Survey results indicated an overall prevalence rate of goitre ranging from 4 to 68.6% and with a mean of 25.1%. It was also observed that areas of high altitudes (over 2000 metres) appear to be more affected than those at low altitudes. In the latest survey of goitre conducted in 10 urban and 12 rural sites in seven regions of the country, a total of 12,703 household members aged 1 - 60 years and 8,052 school children aged 6 - 18 years were studied (ENI, 1988). The results of this study revealed that the goitre prevalence rates in the urban and rural areas ranged from 1.92 to 58.86% and 0.16 to 73.55% respectively. Urinary iodine excretion levels varied from 22.38 to 142.44 µg/day in the urban sites and 10.35 to 97.88 µg/day in the rural areas. For the first time, the study attempted to establish a relationship between urinary iodine excretion values and goitre prevalence. Even though the report claimed an apparent correlation between the two variables, it was not supported by statistical analysis.

Most of the goitre survey reports conducted in Ethiopia attributed the high prevalence of goitre to low iodine availability. There is however, no information about the iodine content of local foods and drinking water. The goitrogenic effects of some foods and the type of drinking water still remain speculative.

In general, almost all goitre studies in Ethiopia have so far focused mainly on determining the prevalence of the problem in various regions. Available information is nevertheless sufficient to recognize goitre as a problem of public health significance in the country. On the other hand, the widely accepted speculation about the cause of goitre in communities in the goitre endemic areas needs scientific verification. It would thus be beneficial to undertake further investigations to identify factors associated with endemic goitre and validate or invalidate these speculations.

1.3 Study Objectives

1. To determine if there is a significant relationship between iodine intake (expressed by urinary iodine excretion) and the occurrence of visible goitre in school children in Sidamo region, South Ethiopia.
2. To determine the factors associated with the occurrence of endemic goitre in the school children, i.e., type of drinking water, dietary

pattern, nutritional status and fluorosis.

1.3.1 <u>Study Sub-objectives</u>

1.1 To identify children with visible goitre and without goitre.

1.2 To determine the urinary iodine concentration levels in the goitrous and non-goitrous children.

2.1 To determine the type of water sources for the goitrous and non-goitrous children in terms of whether the sources are protected or unprotected, treated or untreated.

2.2 To determine the frequency of consumption of commonly consumed foods by the goitrous and non-goitrous school children in the study area.

2.3 To determine the nutritional status of the goitrous and non-goitrous school children.

2.4 To detect the presence of fluorosis in the goitrous and non-goitrous children.

1.4 <u>Hypothesis</u>

1. The iodine intake, as measured by urinary iodine excretion, of children with visible goitre is significantly lower than that of non-goitrous children.
2. Children who get their drinking water from unprotected water sources have a significantly higher risk of endemic goitre than those who get their drinking water from protected sources.
3. Children who get treated drinking water supply have a significantly higher risk of endemic goitre than those who get untreated water.
4. Frequent consumption of certain common foods in the study area exposes children to a significantly higher risk of endemic goitre than those who do not consume or with low frequency of consumption of these foods.
5. Stunted Children (below -2S.D height for age have a significantly higher risk of endemic goitre than those who have normal growth (above -2 S.D height for age).
6. Children who have fluorosis are at a significantly higher risk of endemic goitre than those who do not have these nutritional problem.

1.5 Benefits of the Study

Although there have been many endemic goitre prevalence surveys in Ethiopia, the role of other factors other than iodine deficiency in the etiology of goitre has not been investigated. The results of this investigation will, therefore provide a foundation upon which other in depth studies on goitre can be triggered in highly endemic areas of the country. It is also expected to help to design appropriate intervention techniques which can be incorporated in the national goitre control programme ,so that goitre and its associated disorders could be totally eradicated.

CHAPTER TWO

LITERATURE REVIEW

2.1 Endemic Goitre and Iodine Deficiency

It is generally accepted that iodine deficiency is the dominant factor in the development of endemic goitre. Two observations, however, indicate the existence of factors other than iodine deficiency in the etiophatogenesis of endemic goitre. First, iodine deficiency does not always result in endemic goitre. Second, there are situations in which a significant number of goitres remain and new cases occur in spite of adequate iodine supplies (Gaitan *et al*., 1986).

Studies which have been performed in goitrous and non-goitrous inhabitants of the endemic areas of central Greece (Malamos *et al*., 1966) and eastern Kentucky (London *et al*., 1965) have indicated that all the goitrous and non-goitrous inhabitants have low iodine intakes. The difference in thyroid gland size between the goitrous and non-goitrous populations suggested the existence of factors other than iodine deficiency.

Several investigators have revealed situations of high and low prevalence rates of goitre in nearby localities with equally low iodine intake. Epidemiological surveys conducted within small geographical areas in the Andean region of Colombia (Gaitan *et al*., 1978), Venenzuela (Roche,1959), western New Guinea (Choufoer et al., 1965)

Ecuador (Rodrigo *et al*., 1969), island of Idjwi,Congo Republic (Delange *et al*., 1968) showed that there was a remarkable difference in goitre prevalence among nearby localities ranging from 5% to 58%. These investigators concluded that iodine deficiency could not explain the marked differences in goitre prevalence. This implies that other factors exist that contribute to the difference in goitre prevalence.

As reviewed by Gaitan *et al* (1980), supplementing the diet with iodine resulted in a pronounced decrease in goitre prevalence in Switzerland, New Guinea, the Himalayas, New Zealand, Guatemala, Colombia and Ecuador. The effects of iodine prophylaxis against endemic goitre have also been investigated in the Cauca valley, Colombia (Gaitan *et al*, 1968; Gaitan *et al*., 1978), Tasmania, Australia (Clements *et al*., 1968) and Central Africa (Thilly *et al*., 1973). Contrary to the above observations the results of these studies have demonstrated that the prolonged iodine prophylaxis has not significantly prevented goitre in the population indicating the presence of additional factors other than iodine deficiency.

An investigation conducted on the problem of goitre in Ceylon has indicated, quite surprisingly, that the iodine content of the food of people even in areas where goitre is endemic is about 300-350 μg per person per day, whereas in the non-endemic area, is about 850 μg per day (Mahadeva *et al.*, 1968). This was well above the allowed average daily intake (100-150 μg) of iodine per person. Dietary surveys and radioisotope studies in Northern Virginia have also shown that iodine intake can be adequate even when endemia is observed (Vought *et al.*, 1967) .

It may therefore, be concluded that iodine deficiency plays an important role in the development of endemic goitre and that iodine supplementation is an effective public health measure in substantially reducing prevalence rates and minimizing the risk of goitre development in many people. However, there is sufficient evidence to show that factors other than iodine deficiency act in a synergistic manner to produce a goitre endemia.

2.2 Endemic Goitre in Relation to Goitrogens in Foodstuffs

Although the idea that certain foods may cause thyroid enlargement has existed for many years, the findings of Chesnay, Clawison and Webster in 1928 have been considered as the first milestone towards progress in this field (Greer and Astwood, 1948). These investigators discovered that rabbits being maintained in their laboratory developed large goitres while on a daily ration of cabbage. After considering other factors which might have been responsible, they concluded that the cabbage was the etiologic agent.

Greer et al., (1949) cited an earlier report which indicated that during the second world war, in Belgium, the prevalence of goitre increased from 16% to 26% due to the high consumption of cabbage and similar vegetables. Suk's (1931) study was cited by the same author to have stated that the goitrous population of Carpathian Ruthenia in Switzerland lived practically on cabbage. A further survey of the activity of Brassica seeds has reported that seeds of Brassica produce thyroid enlargement when fed to rats (Kennedy and Purves, 1941).

A review by Greer and Astwood (1949), cited that a variety of foods, including chard, rape, turnip (Hercus and Purves, 1936), soybeans (Sharless, 1938; McCarrison, 1934), and peanuts (McCarrison, 1937) have been observed to cause goitre in both laboratory animals and livestock.

The antithyroid effect of sixty-one foods was tested in one hundred different subjects using radioactive iodine (Greer and Astwood, 1948). Of the foods tested, rutabaga or yellow turnip was found to posses the greatest antithyroid activity. In general, foods belonging to the vegetable kingdom were more active than animal products with the most potent vegetable families being the Chenopodiaceae, Compositae, Cruciferae, Cupuliferae, Juglandaceae, Leguminosae, Rosaceae and Umbelliferae. In the animal products, Cow milk, beef liver, and oysters have been shown to have some activity.

A study on the goitrogenic effect of groundnut on albino rats has revealed that arachidoside, a glucoside isolated from the red skin of groundnut produces a typical colloid goitre (Srinivasan et al., 1957). Further experimental studies by Moudgal et al. (1958) have demonstrated that the inclusion of pigments; arachiodoside from groundnuts, anacardioside from cashenuts , anthocyanin from almonds and catechin from areca nuts, in the diet of rats results in goitre.

Two goitre endemias have indicated the presence of goitrogenic substances in milk. One was in Tasmania where a seasonal increase in goitre prevalence appears to coincide each year with the spring flush of pastures and weeds in spite of adequate iodine intake (Clements, 1968). It was postulated that milk which was consumed in large amounts by young children, had a goitrogenic substance from the cruciferous weeds eaten by the cows. The other endemia cited was in Finland in which goitrin, a thiglycoside present in cow milk from the region of endemic goitre, has been considered the causative factor (Gaitan, 1980). It was observed that rats fed for one to two years on milk produced in endemic goitre districts had thyroid glands which were almost twice as large as those from rats fed milk from non-goitrous districts. It was thus concluded that goitrin, in cow milk could be responsible, at least in part, for the goitre endemia in those areas of Finland.

A series of tests on human volunteers fed on milk obtained from cows fed on different types of rations were conducted (Clements, 1960). The results showed that milk from cows feeding on some crops or pastures like chou moellier, interferes with uptake of iodine by the thyroid. The presence of goitrogens in some pastures has also been reported in New Zealand where epidemic (epizootic) of goitre occurred in new born lambs and ewes which had been feeding on some pastures and turnips, respectively (Purves and Frsnz, 1974).

Experimental observations conducted in Lebanon have indicated that propyl disulphide, the main volatile constituent of onions inhibits thyroid function significantly as it was shown by the low values for uptake of iodine in rats treated with the chemical (Saghir et al., 1966). The study suggested that the consumption of onions may contribute to the incidence of goitre in Lebanon where onions are consumed in great amounts by the people.

The goitrogenic role of cassava has been evidenced in the etiology of two endemias. Studies in Zaire have shown that the ingestion of cassava grown in the northern goitrous area results in a decreased thyroidal radioiodine uptake, while that grown in the non endemic areas does not affect iodine uptake (Ermans et al, 1983). Concomitantly, people living in the goitrous area were observed to excrete large amounts of thiocyanate in the urine than those living in the non-goitrous area. The investigators attributed the action of cassava to the endogenous release of thiocyanate (SCN) from linamarin, a cyanogenic glucoside contained in cassava, in particular in the tuberous roots. A survey in Eastern Nigeria has revealed that those towns and villages with the highest incidence of goitre are those feeding mostly on dry unfermented cassava (Ekpechi, 1967). The authors from both countries have mentioned studies on rats which showed that repeated feedings with cassava grown in the endemic areas of Zaire and eastern Nigeria induce changes in iodine metabolism.

In rural Sudanese villages where the staple diet consists solely of millet, the goitre prevalence in school children was 75% while in towns where the diet consists of a combination of millet, durra (Sorghum Vulgare), and wheat (Triticum Vulgare) the prevalence was low. A thionamide like substance was isolated from the millet meal and a high concentration of the same substance was found in the serum of the school children in the highly endemic villages where millet was the main staple food

(Osman, 1981). Based on the above mentioned observation and experimental data on rats goitrogenic substances in Bulrush millet (Pennisetum typhoides) cultivated in different parts of Sudan have been postulated as contributory factors to the endemicity of goitre in Western Sudan (Osman and Fatah, 1981). In a review, Osman (1981) has cited similar studies done in Cameroun, Nigeria and India which associated millet with endemic goitre.

2.3 Endemic Goitre in Relation to Water Supplies

There are many descriptions of goitre that have been attributed or related to bacterial and chemical pollution of drinking water supplies.

Results of bacteriological studies carried out in 21 of the 41 localities in western Colombia have provided some evidence that the overall concentration of bacteria in the pipeline system is related to a higher goitre prevalence (Gaitan et al., 1980). In the same country, studies were conducted to determine the effect of water treatment on goitre prevalence (Gaitan, 1973). In two towns, significant decreases in goitre prevalence was observed after modern water treatment plants were put in operation. This observation implies that pollution of water with microorganisms was a contributory factor to the endemia.

An epidemiological study conducted in northern Virginia to test the hypothesis that the prevalence of thyroid enlargement is related to the type of water supply furnished to the population (Vought *et al*., 1967). The results of this study revealed goitre prevalence among those using dug wells (30.9%) was significantly higher ($p<0.025$) than those using the public supply (20.4%). Cell-free broth cultures from polluted spring which supplied a highly goitrous population in Northern Virginia have indicated that E. Coli contains an antithyroid compound (Vought *et al*., 1974). The name of the antithyroid compound and its mechanism of activity were however, not been given.

Studies conducted in 37 localities in Western Colombia have indicated that towns located downstream from sedimentary rocks, rich in organic matter, have the highest goitre prevalence. In contrast, those populations taking their drinking water from streams flowing across igneous rocks, devoid of organic matter, show a low goitre prevalence (Gaitan *et al*., 1978). Another investigation has also yielded the same observations in other localities (Gaitan *et al*., 1980). These observations suggest that organic matter from sedimentary rocks is the goitre causing factor in drinking water. Gaitan *et al*. (1986) in a paper which reviews goitrogenic factors, cited studies on organic goitrogens in water. Over 30 organic compounds containing antithyroid activities were identified by ultrafiltration and chromatography of water extracts from a goitrogenic well of Candelaria town in western Colombia. Only four compounds were identified in the extracts from a non-goitrogenic well water, which supplied the district of Candelaria where goitre prevalence is low. Other studies were also mentioned which identified organic compounds from the goitrogenic well with potent antithyroid activity.

In Greece, it has been shown that villages without endemic goitre have drinking water coming from deep layers (Malamos et al., 1971). In villages with endemic goitre, the drinking water came from superficial sources which contained significantly less total salts, iodine, chloride, carbonate, bicarbonate, sodium and zinc, and it was significantly more often polluted with Escherichia Coli and Coli-like organisms. From the above observations, it is possible to imply that endemic goitre in Greece correlates with several water characteristics.

Studies in Trujillo State, Venezuela have documented higher lithium (Li^{+}) concentration in the water supply of a high incidence endemic goitre locality than in that of nearby non-endemic communities (Gaitan et al., 1986). These authors mentioned other experimental observations which indicated that Li^{+} at those concentrations could be goitrogenic.

In a review by Ramalingaswa *et al.*, (1961) on the etiology of Himalayan endemic goitre the early works of two investigators have been mentioned. The first medicotopographical studies cited were conducted in India in 1835 by McClelland which suggested that the high calcium content of drinking water may be the causal factor. The other study mentioned was by Stott who worked in one part the Himalayan endemic zone and has indicated that drinking hard water containing excessive amounts of calcium is of etiological importance. Other studies have also shown that there is a close correlation between the degree of water hardness and goitre prevalence (Day and Jackson, 1972).

Epidemiological studies in Western Colombia have explained the influence of water supplies on the frequency of goitre. One of the studies has pointed out that in the City of Cali, children living in the area supplied by the Cali river have a significantly higher ($P < 0.001$) prevalence of goitre than those living in the area supplied by the Cauca river (Gaitan, 1973). An other similar study demonstrated that water from the well in the northern part of Candelaria in contrast with water from the southern part causes thyroid enlargement and decreases thyroid iodine content (Gaitan *et al.*, 1978). All the investigators, however, did not attribute the goitrogenic action of the water sources to any chemical or bacterial contamination. It may therefore, be suggested that the main factor underlying endemic goitre in western Colombia is not nutritional iodine deficiency but some contaminants in the water supplies.

2.4 Endemic goitre in relation to fluorosis

Fluoride may be another important factor to goitre development. However, epidemiological evidence of an association between fluoride and endemic goitre is contradictory. While areas in which the water contains an unusually high level of fluoride or in which dental fluorosis is pronounced have been shown to coincide with the regional distribution of goitre, the absence of endemic goitre in other areas where the fluoride levels are equally high has been noted (Day and Jackson, 1972). It is suggested that a high intake of iodine may offset the goitrogenic effect of fluoride, which might explain the absence of goitre in some high fluoride areas. The same investigators conducted a study in 17 Himalayan villages to determine the relationship between fluoride and endemic goitre. The findings revealed that the wide variations in goitre prevalence correlate closely with the fluoride content of the water in each village. It has been observed that the lowest goitre prevalence occurs in low fluoride water villages, whilst goitre prevalence is higher when the water contains more fluoride.

A relationship between goitre and fluorosis has been suspected in Kenya (Editorial, 1982). This is based on the observation that some areas which suffer from endemic goitre in Kenya also have the highest prevalence of fluorosis in the country. Thus, the author has hypothesized that endemic goitre in Kenya could be a consequence of relative iodine deficiency in the central highlands where there is a simultaneously relative abundance of fluoride. These associations are unlikely to be due to chance. The mechanism in which fluoride produces goitre has not been clearly explained by any investigator.

2.5 <u>Endemic Goitre in Relation to nutritional status</u>

Goitre and growth retardation are believed to be two important consequences of iodine deficiency and a frequent question has been whether the two are related. Both have been speculatively attributed to hypothyroidism, the goitre as a response to increased thyroid stimulating hormone (T.S.H), and the growth retardation from deprivation of the thyroid hormone essential for normal development (Barzelato and Covarrubias, 1969). There has been much uncertainty in the literature as to whether growth is related to the incidence and size of goitre in endemic areas. Separate studies from different countries have addressed this subject, with differing conclusions as to whether or not a positive relationship exists.

Bautista *et al.* (1977) have reviewed some of the studies on the relationship of thyroid size and body growth. In his review paper, a study in Nepal has been cited to find less retardation of height in goitrous cretins than in non-goitrous ones. Another investigation which compared goitrous children with non-goitrous ones living in the same village in areas of mild goitre endemicity in Greece demonstrated that there are no differences in height, weight, skin fold thickness or bone age in these two groups. However, it has been reported that both groups are significantly smaller by each of these measurements than children living in non-endemic areas of the country. The same paper cited observations which have been made on 408 children in highland Bolivia. The findings have shown that the presence or size of goitre has no consistent correlation with height, weight or head circumference. Another study cited on the paper which was an extensive survey of over 19,000 school children in Zagreb, Yugoslavia, indicated that children with large goitres are, on the average, taller and heavier than those with small goitres, who were, in turn, taller and heavier than those without goitres. A study, involving adult Indians of Pedregoso in the Chilean Andes has pointed out a significant correlation between increasing goitre size and height, although non-goitrous men of the same age are, in general, taller than goitrous one (Barzelatto and Covarrubias, 1969).

In Greece, a study of nutritional status, growth and skeletal development was conducted in 395 goitrous and 314 non-goitrous children living in four villages with endemic goitre and compared to 493 non-goitrous children living in three goitre-free villages (Koutras et al., 1973). The study showed that the children in the goitre endemic villages have a lower body height, a smaller body weight, a thinner skin fold, and delayed bone maturation than the children living in the goitre-free villages. In the same study, 81 goitrous and 198 non-goitrous men more than 40 years old and living in six villages with endemic goitre were compared with 119 non-goitrous men from two non-goitrous villages. The results have indicated that the non-goitrous are shorter but heavier and with a large skin fold than the men living in the endemic areas.

In summary the studies described in this paper emphasize the complex and multifactorial etiology of endemic goitre. The important role of iodine deficiency as an etiologic factor in endemic goitre is well established, but there is evidence that other environmental factors can play an equally important role in the pathogenesis of this condition.

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study Design

This investigation was a case control study in which individual cases and controls were matched for age and sex. The major aim of the individual matching was to avoid bias that might arise from age and sex dissimilarities of the case and control populations. The investigation involved clinical examination of goitre, fluorosis and laboratory analysis of iodine in urine, anthropometric measurements and administration of a questionnaire.

1.6 Study Site

This study was conducted in Sidamo administrative region, in the southern part of the country. The study area is located in Awassa Zuria district, bordering the town of Awassa which is the capital town of the region. Awassa town is about 300 kilometres away from Addis Ababa. The six schools at which the study was conducted are located along the road which runs from Awassa to Yirgalem, another town south of Awassa. Out of the six schools, the nearest to Awassa (Gimbigenet) is only five kilometres away along the main road and extends two kilometres to the left of the road. The farthest school (Aramfama) is 20 kilometres away from Awassa, including the five kilometres that branch from the main road.

Previous data (ENI, 1988) has indicated that in the study area (less than 11 kilometres long) there are marked differences in goitre prevalence among children from different schools. Thus, this area was found appropriate to investigate factors that brought about the difference among the school children in the area.

3.2 Study Population and Sample Size

The study population consisted of school children 6 - 18 years of age attending six schools in the study area. This group is selected because of its accessibility and relatively high risk of goitre within the population.

From a preliminary survey of the school children in the study area, it was found that 5% of the non-goitrous children do not belong to the indigenous ethnic group of the study area. This was apparently the lowest rate of prevalence for the factors which were included in this study. For determination of minimum sample size needed for this study, the 5% rate was therefore taken into account. To detect a difference if each factor was associated with a three-fold increase of goitre (Odd Ratio = 3) and to give a 90% power (1.28) of achieving 5% significance (1.96), the sample size was calculated from the following formula:

$$n = \frac{(U\sqrt{[\Pi_1(1-\Pi_1)+\Pi_2(1-\Pi_2)]}+V\sqrt{[\bar{\Pi}(1-\bar{\Pi})]})^2}{(\Pi_2-\Pi_1)^2}$$

π_1 = Proportion of controls exposed

π_2 = Proportion of cases exposed, calculated from

$$\pi_2 = \frac{\pi_1 OR}{1 + \pi_1 (OR - 1)}$$

u = One sided percentage point of the normal distribution corresponding to 100% - the power.

v = percentage point of the normal distribution corresponding to the (two-sided) significance level

Therefore:

$$n = \frac{[1.28\sqrt{(0.5 \times 0.95 + 0.136 \times 0.864)} + 1.96\sqrt{(2 \times 0.093 \times 0.907)}]^2}{(0.136 - 0.05)^2}$$

$= 236$

The sample size required in this study was therefore 236 goitrous children and 236 non-goitrous children who were individually matched for age and sex. A rapid preliminary survey of the school children indicated that at least 20% of the non-goitrous children in the study area were exposed to the remaining suspected factors under investigation. It was therefore possible to use the same sample size to detect a difference if each of these factors was associated with a twofold increase of goitre (odd ratio = 2). The sample size required when a 20% rate and a two-fold increase were considered was 238 goitrous and 238 non-goitrous children.

Urinary iodine concentrations were measured in 28 goitrous and 28 non-goitrous children who were matched by age and sex. Statistically, this number was reported to allow for changes in urinary iodine concentration arising from possible differences in dilution from one urinary sample to another (Dunn and Vander-Haar, 1990).

3.3 Sampling

In the preliminary clinical assessment of goitre, 235 children with visible goitre (grade 2 and 3) and 770 non-goitrous (grade 0) children were identified out of children in the six schools. Those children with non-visible goitre (grade 1A and 1B) were not included in the study. The 235 children with visible goitre and 770 non-goitrous children were stratified by age and sex into 40 groups, i.e., each stratum consisted of children of the same age, sex and goitre status. For each child in the 20 strata of the goitrous group, serial numbers were given based on which identity numbers were allocated. The sequential order of the identify number was determined by using random number tables to pick each serial number at a time. The non-goitrous children in each stratum were also given serial numbers. For each of the stratum of the goitrous children one child was picked at a time following the sequence of the identity numbers and was matched with another non-goitrous child who was singled out randomly from the corresponding stratum in the non-goitrous group and was given the same ID number as the goitrous child. This matching process continued until all the 235 cases were completed and the remaining non goitrous children were excluded from the study.

Urinary iodine concentration levels were determined in the urine of 28 children with visible goitre and 28 children without goitre who were sub-sampled by systematic random sampling from the 235 matched pairs.

3.4 Field Study Instruments

3.4.1 Questionnaire

This was a structural questionnaire which was administered to the mother of the child or caretaker. It consisted of questions on demography, source and quality of drinking water and frequency of commonly consumed foods by the child. A sample of the questionnaire is presented in Appendix 7.

3.4.2 Height Measuring Equipment

A stadiometer with a flexible measuring tape graduated in centimetres was used for measuring height.

3.5 Training of Interviewers

Enumerators were recruited among candidates who had completed high school. These were previously involved in other similar field studies in the area. All of them were fluent in Sidama and Amharic, which were the languages spoken in the study area. An intensive training of one week was given which consisted of a thorough review of the questionnaire, direction as to how to fill in numbers clearly and legibly, how to accurately calculate age and to measure height properly.

3.6 Pilot Study

The pilot study was done in two schools at Yirgalem town in Sidamo administrative region. This area borders the study area and is similar in all respects to it. Forty cases with their individually matched controls were covered during the pilot phase. A draft questionnaire was administered to each child's mother or female caretaker, to test its clarity, length, acceptability, reliability and ease of analysis. Height measurements were made for all cases and controls. The appropriateness of the sampling procedures were also evaluated practically.

The results of the pilot study were discussed by advisors and academic staff of the Unit of Applied Nutrition and relevant adjustments were made, especially for the food frequency questionnaire.

3.7 Data Collection

3.7.1 Interviewing Procedure

Each study child was requested to identify his village number, house number and the name of the head of the household. Based on this information, enumerators were able to pinpoint most of the children's households with the help of the community guides. For a few households which were located deep in the rural areas, the enumerators were accompanied by the study children. On arriving at a household the enumerators introduced themselves and established rapport with the respondent. The mother or female caretaker of the child provided all the responses.

3.7.2 Height Measurement

Standard procedures of height measurement were used taking the necessary precautions. The child was asked to stand straight and look straight ahead on a flat surface. The heels were maintained together and the body was placed so that the shoulder blades, buttocks, and heels touched the vertical surface of the heightmetre. The feet were maintained flat on the floor, slightly apart with the legs and back straight and arms at the sides. The head was held comfortably erect, with the lower border of the orbit of the eye in the same horizontal plane as the external canal of the ear. The headpiece of the stadiometer, was gently lowered, crushing the hair and making contact with the top of the head. The height was directly read from the headpiece of the stadiometer.

3.7.3 Determination of Age of Child

The mothers or caretakers were helped to remember the dates of birth of their children by using a local calender of events. The calculated ages were recorded to the nearest year.

3.7.4 Clinical Examination

Clinical examinations of goitre were carried out on all school children at the six schools who were present during the preliminary assessment. The clinical examinations for goitre were done in accordance with the grading system endorsed by the World Health Organization and the International Council for Control of Iodine Deficiency Disorders (Dunn and Vander-Haar, 1990). All examinations were done by the investigator under the direction of an experienced medical doctor.

For examination of the children, palpation was used. The examiner stood or sat facing the subject, placed his two thumbs on either side of the subject's windpipe several centimetres below the notch of the thyroid cartilage (the "Adam's apple") and rolled his thumbs gently over the thyroid, which lies next to the windpipe

If each lobe of the thyroid was smaller than the part of the subject's thumb beyond the last joint (the "terminal phalanx"), the goitre was classified as <u>Grade 0, no goitre</u>. If each lobe was larger than the terminal phalanx of the subjects thumb, he or she had goitre.

To define the goitre size, the subject's head was tilted back and the examiner tried to see the goitre. If it could not be seen but was palpable, the goitre was classified as <u>Grade 1A</u>. If the goitre could be seen as well as palpated, the subject's head was returned to the normal position, i.e., looking straight ahead. If the goitre could be seen only with the head tilted back, it was called <u>Grade 1B</u>. If it could be seen with the subject looking straight ahead, it was called <u>Grade 2</u>. If it was quite large and could easily be seen from a distance of about 10 meters, it was called <u>Grade 3</u>. Grades 2 and Grades 3 were collectively called visible goitre. These two plus grades 1A and 1B were considered to make total goitre.

Each study child was examined for presence of clinical signs of fluorosis by the medical doctor and the findings were recorded.

3.8 <u>Measurement of Iodine in Urine</u>

<u>Introduction:</u> The urinary iodine concentrations were determined according to the method of Gutekunst as modified by Dunn and Crutchfield (1991). The basis for

this method is the Sandell-Kolthoff reaction with some prior step involving digestion of urine with chloric acid under mild conditions. Iodine was colorimetrically detected by ceric sulphate reduction.

Materials, Reagents and solutions: This method required heating block, colorimeter, thermometer, test tubes (13 mm x 100 mm), reagent flasks and bottles, pipettes and laboratory balance. Chemical reagents required were $KClO_3$, $HClO_4$ AS2O3, NaCl, H_2SO_4 $Ce(NH_4)_4(SO_4)_4 . 2H_2O$, H_2O and KIO_3 Solutions used during the analysis were chloric acid solution, arsenious acid solution, ceric ammonium sulphate solution and standard iodine solution. Procedure for the preparation of the solutions are given in appendix 1.

Procedure: Each urine sample was mixed to evenly suspend any sediment and 250 µl of each was pipetted into a 13 x 100 mm test tube. For a blank, 250 µl of H_2O was pipetted into 13 x 100 mm test tube. From the prepared stocks, 250 ul of each iodine standard (2, 4, 6, 8, 15, 20, ug/dl) was pipetted into 13 x 100 mm tube. To each test tube containing samples, blank and standards, 750 ul of chloric acid solution was added and was mixed gently. All tubes were heated, for 50 - 60 minutes in a heating block at 110 - 115° in a hood with perchloric acid trap. These were then cooled to room temperature. 3.5 ml arsenious acid solution was added to each tube and mixed by inversion. All tubes were left to stand for about 15 minutes and then 350 µl of ceric ammonium sulphate solution was added at intervals of 30 seconds between the tubes and quickly mixed. Exactly ten minutes after addition of ceric ammonium sulphate to the first tube, its absorbency at 405 mu was read in colorimeter, and successive tubes were read at 30 seconds interval.

To calculate the results, a standard curve was constructed by plotting iodine concentration of each standard (abscissa) against its spectrophotometer reading (ordinate). The standard curve used in this study is given in Appendix 2 . For each sample, the spectrophotometric absorption was found on the standard and then corresponding iodine concentration on the abscissa located. This was the value of urinary iodine concentration in µg/dl.

3.9 <u>Data Cleaning, Processing and Analysis</u>

The questionnaires completed each day were examined in the field, to check for completeness of data, consistency of answers and measurements obtained, and for proper filling of the forms by the principal investigator. Data from completed questionnaires and laboratory results were entered into computer using DBase III Plus computer programme at the ANP. Data cleaning was carried out to ensure that data had been entered correctly into the computer.

Different computer programmes were used in the data analysis. Frequency of variables and cross tabulations were done by SPSS/PC. Determination of odd ratios for the matched case control pairs and tests of significance by McNemars's Chi-square were done by Epi Info Version 5. CDC was used for anthropometric data, height.

CHAPTER 4

RESULTS

4.1 Prevalence of Goitre in School Children.

Table 1 gives the prevalence of goitre in school children by sex and age-group. A total of 2013 school children in six schools were examined in the preliminary assessment of goitre in the study area. Of these, 1346 were males and 667 females. The overall prevalence of goitre was 61.7%, (68.2% in females and 58.5% in males). Fifty percent of those with goitre were either grade 1A or 1B. The prevalence of visible goitre was 11.7%, with a rate of 18.1% in females and 8.5% in males. There was, however, a marked difference in total and visible goitre prevalence among the six schools ranging from 51.2 to 77.1 and 5.4 to 19.5, respectively (Figure 1).

Table 1: Goitre Prevalence in School Children by sex and age Groups

Sex	Age Group	No. Examined	Goitre Prevalence Total	Goitre Prevalence Visible
Male	6-8	125	79(63.2)*	9(7.2)
	9-11	607	370(60.95)	52(8.6)
	12-14	467	275(58.9)	48(10.3)
	15-17	147	64(43.5)	5(3.4)
	Total	1346	788(58.5)	114(8.5)
Female	6-8	85	59(69.5)	10(11.8)
	9-11	228	158(69.3)	45(19.7)
	12-14	222	154(69.4)	37(16.7)
	15-17	132	84(63.6)	29(2.2)
	Total	667	455(68.2)	121(18.1)

* Figures in parenthesis are percentages

Distribution of children by school and goitre prevalence (N=2013)

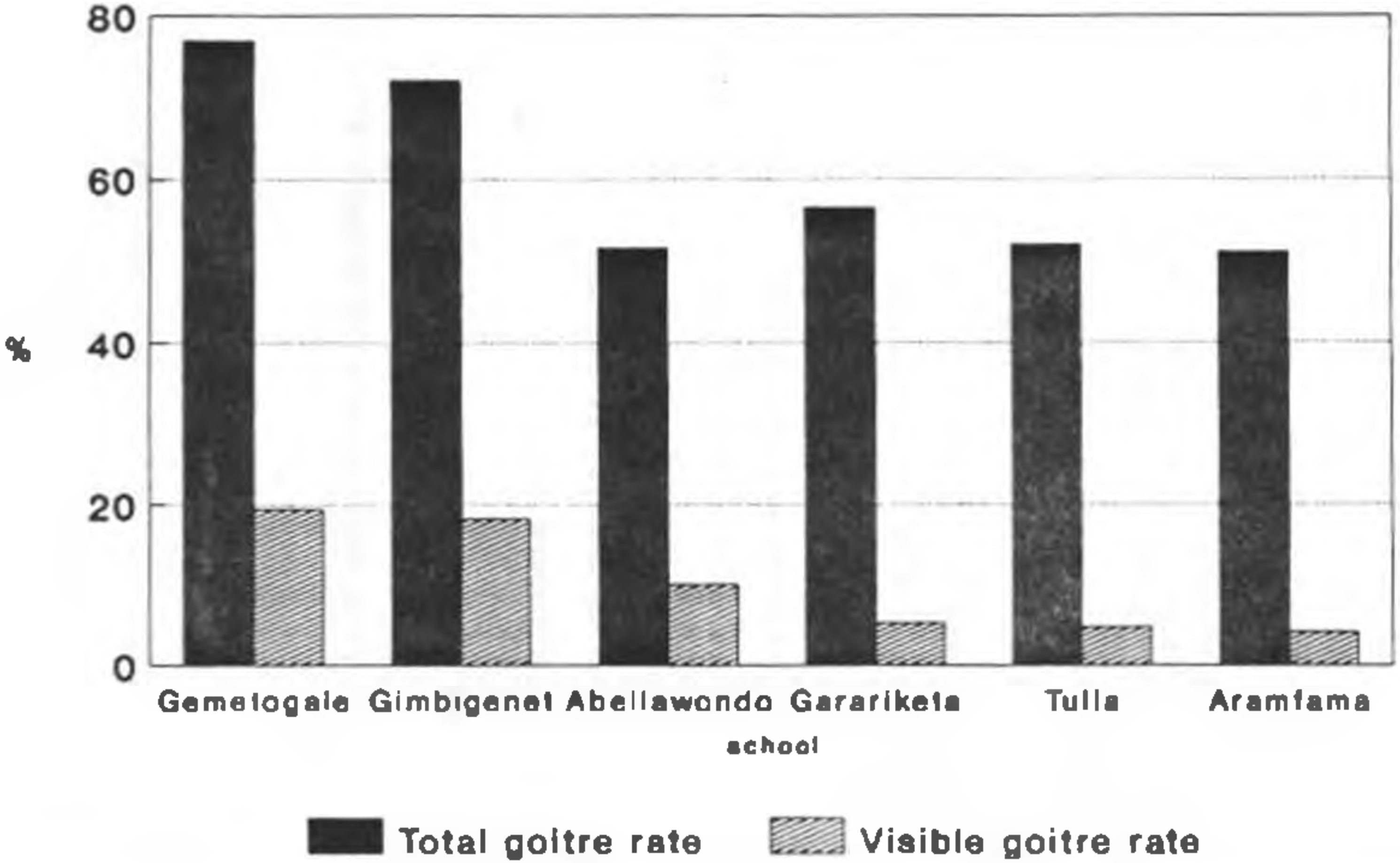

Figure 1

Out of the 2013 children, 235 (11.7%) children with visible goitre were identified and individually matched by sex and age to 235 children without goitre for further study. Of these children with visible goitre, eighty-six percent were from three schools, namely, Gimbigenet, Gemetogale and Abellawondo. Out of the 470 study children 228 (48.5)) were males and 242 (51.5%) were females.

4.2 Factors associated with endemic goitre in school children.

4.2.1 Iodine intake

The distribution of samples by urinary iodine excretion levels and by the goitrous and non-goitrous study children is given in Table 2.The concentration of iodine in urine is used as a biochemical marker of iodine intake. The mean urinary iodine concentrations in both the case and control groups of this study were 16.2 µg/dl, with standard deviations of 9.7 and 9.9, respectively. More than 80 percent of the urine samples showed iodine concentration levels above 10 µg/dl.

Table 2: Distribution of urine samples with typical values for iodine concentrations by the two study groups.

Study Group	Number examined	Urinary Iodine Concentration (µg/dl)			
		<2	2-5	5 - 10	>10
Non-goitrous	28	0	1 (3.6)*	4 (14.3)	23 (82.1)
Goitrous	28	0	1 (3.6)	5 (17.9)	22 (78.6)

* Figures in parenthesis are percentages

a.2.2. <u>Type of foodstuffs</u>

The main staple foods of the study area were Enset, maize and teff <u>(Eragrostis abyissinca)</u>. The frequency of consumption of the common foods in the study area by the two study groups is presented in figure 2 and appendix 3.

Only teff and sugarcane were consumed at a significantly higher rate by the children with visible goitre than those without goitre. Based on this finding, only the association of the high consumption of teff and sugarcane with endemic goitre occurrence was tested in this investigation.

Frequency of consumption of commonly consumed foods by the case-control groups

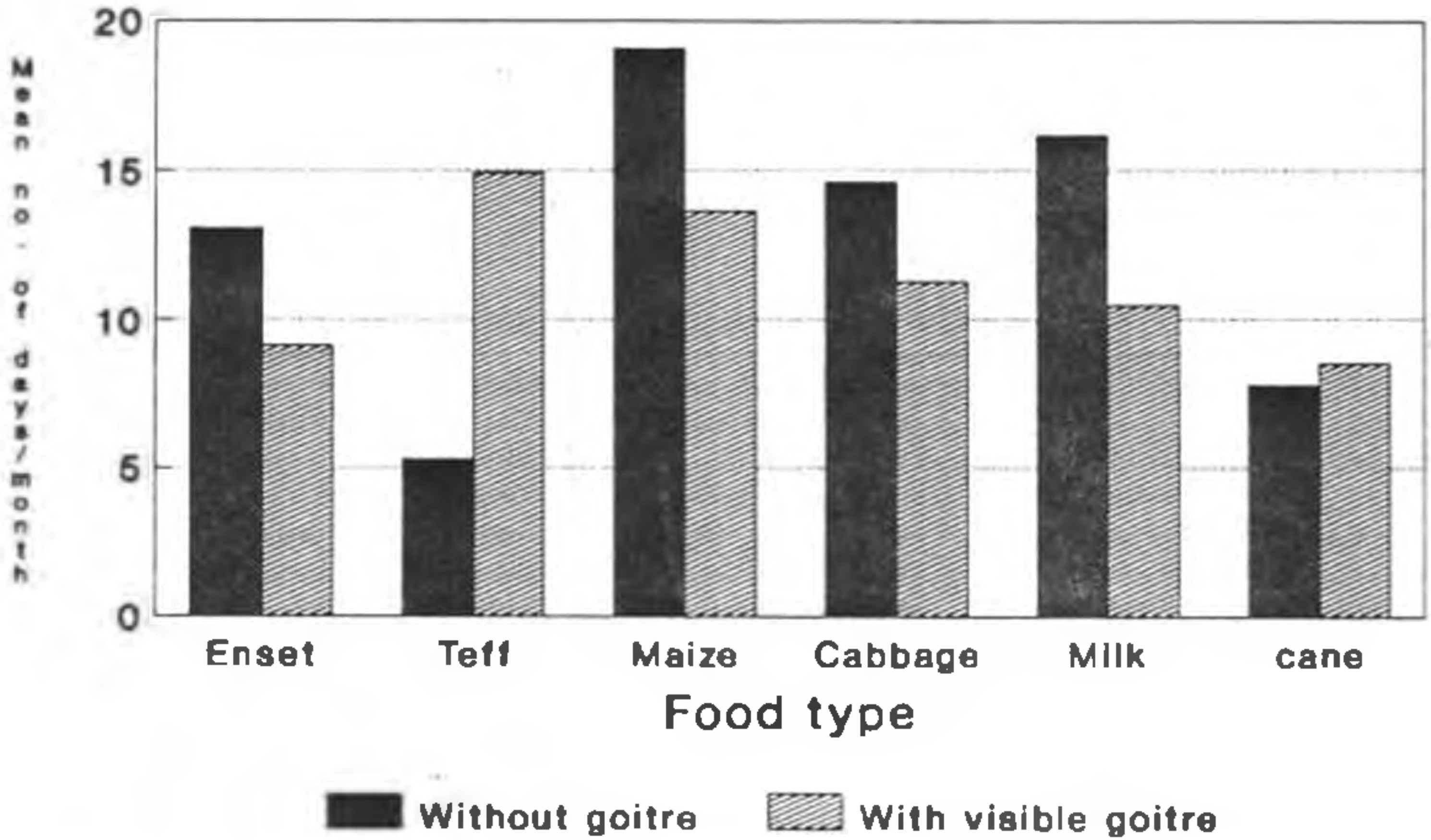

Figure 2

4.2.2.1. *Teff*

Daily consumption of teff was taken as a risk factor because there was a clear cut difference between this and the other frequencies of teff consumption among the study children. Seventy seven percent of the study children either did not consume teff or consumed it only one to three days per week and only three percent had a frequency of four days per week while the remaining 20% consumed it daily. Table 3 shows the results of the age and sex matched pair analysis in which the everyday consumption of teff was greatly associated with the presence of visible goitre in the study children. The odd ratio was 19.5 with a 95% confidence limits of 9.6 to 24.2. The McNemar's Chi-square test, for the correlated proportions, indicated that the difference in goitre occurrence between the children who consumed teff daily and those who did not do so was very significant (P<0.0001).

Table 3: Everyday consumption of teff and risk of endemic goitre:matched analysis.

		Non-goitrous	
		Teff used everyday (n)	Teff not used everyday (n)
Goitrous	Teff used everyday	6	78
	Teff not used everyday	4	147
	Total	10	225

OR = 19.5 X^2 = 64.98 D.f = 1 P <0.0001)

When unmatched analysis of the same data, from the matched pair case-control study of every day consumption of teff and endemic goitre was done, the odds ratio was 12.5 with a 95%

confidence limits of 5.91 to 26.24 (Table 4). Chi-square test showed that this association was also significant ($p<0.001$).

Table 4: Every day consumption of teff and visible goitre: Unmatched analysis.

	Goitrous (n)	Non-goitrous (n)	Total (n)
Teff consumed daily	84	10	94
Teff not consumed daily	151	225	376
Total	235	235	470

OR = 12.5 X^2 = 71.28 d.f = 1 P < 0.001

The dietary pattern of the study children was related to their ethnic origin. Cross tabulations and chi-square test indicated that there were significant differences in the frequency of consumption of the common foods in the study area between the Sidama and the non-Sidama ethnic groups (Appendix 4). On the other hand, 38.8% of the children with visible goitre belonged to the indigenous sidama ethnic group while 85.7% of the children with visible goitre were from the non-indigenous ethnic groups (Appendix 5). Thus, stratified analysis was done to control the confounding effect of ethnicity in the association of teff consumption and endemic goitre.

As seen in Table 5, an estimated relative risk of goitre associated with every day consumption of teff was 8.00 for the Sidama and 3.49 for the non-Sidama with a 95% confidence limits of 2.45 - 28.93 and 1.03 - 12.19, respectively. A single summary estimate of the association between daily consumption of teff and endemic goitre (Mantel-Haenszel weighted odds Ratio) was 5.51 with a 95% confidence limits of 2.56 to 11.86. The Mantel-Haenszel Chi-Square statistic indicated that the association was significant (P<0.0001).

Table 5: Every Day consumption of teff and risk of endemic goitre, stratified by ethnic groups.

Ethnic Group	Frequency Of teff Consumption	Goitrous (n)	Non-goitrous (n)	Total (n)
Sidama*	Daily	18	4	22
	Not daily	121	215	366
	Total	139	219	358
Non-Sidama**	Daily	65	6	71
	Not daily	31	10	41
	Total	96	16	112

* OR = 8.0 χ^2 = 18.19 d.f = 1 P < 0.001
** OR = 3.49 χ^2 = 5.34 d.f = 1 P < 0.02

4.2.2.2. *sugarcane*

Unlike teff, only a few children with visible goitre and without goitre had a daily consumption of sugarcane. Thus, everyday consumption of sugarcane could not be considered as a risk factor to develop goitre. However, the consumption rate of sugarcane by the children with visible goitre was significantly (p<0.001) higher than the non-goitrous children (Appendix 4). It was therefore, necessary to take a particular consumption rate of sugarcane by the study children as a cut-off point above which sugarcane consumption would be considered as a risk factor. Consumption of sugarcane more than two days per week was taken as a critical point because it was the median consumption rate of sugarcane represented by

56% of the study children. Table 6 shows the number of the matched case-control pairs who consumed sugar cane more than two days per week and those who did below this rate. The odd ratio was 4.4 with a 95% confidence limits of 2.4 to 8.2. McNemar's Chi-square test showed that the difference in the occurrence of visible goitre between the children who consumed sugarcane more than two days per week and who did not do so was significant (P<.001).

Table 6: Consumption of sugarcane more than two days per week and risk of endemic goitre:matched analysis.

		Non-goitrous	
		Consumed Sugarcane > 2 days/ week (n)	consumed Sugarcane ≤ 2 days/ week (n)
Goitrous	Consumed Sugarcane > 2 days/ week	4	48
	Consumed Sugarcane ≤ 2 days/ week	11	172

OR=4.4 X2=21.96 D.f=1 P<.001

When the estimate of the relative risk was calculated from the data with the matched pairs not retained in the analysis, the odds ratio was 4.2 with a 95% confidence limits of 2.18 to 8.07. Chi-square test indicated that the association was still significant (P<0.001)

Sugar cane was consumed at a significantly (P<0.001) high rate by the non-Sidama children (Appendix 5). Consumption of sugarcane more than two times per week was also significantly (P<0.001) associated with the presence of visible goitre (Appendix 4). Thus, as seen in Table 7, an estimate of the association between the consumption of sugarcane more than two times per week and visible goitre was calculated for the Sidama and non-Sidama children separately. The estimated relative risk of goitre associated with the consumption of sugarcane more than two days per week was 4.15 for the Sidama ethnic group and 1.17 for the non-Sidama with a 95% confidence limits of 1.86 to 9.42 and 0.31 to 4.82 respectively.

The pooled estimate of the relative risk (Mantel-Haenszel weighted odds ratio) was 2.92 with 1 95% confidence limits of 1.54 to 5.54. Mantel- Haenszel Chi-square test showed that this association was also significant (P<0.001).

Table 7: Consumption of sugarcane more than two days per week and risk of endemic goitre, stratified by ethnic group.

Ethnic Group	Frequency of sugarcane Consumption	Goitrous (n)	Non-goitrous (n)	Total (n)
Sidanma'	>2days/week	25	11	36
	2day/week	114	208	322
	Total	139	219	358
Non-Sidama''	>2days/week	27	4	31
	2days/week	69	12	81
	Total	96	16	112

* OR=4.15 X^2=15.75 d.f=1 P<0.0001

** OR=1.17 X^2=0.07 d.f=1 P=0.796

4.2.3. Type of Drinking Water Supplies

4.2.3.1. *Treated public water supply*

The distribution of the type of water source between the goitrous and non-goitrous study children is given in Appendix 3. Forty two percent of the 470 study children had treated water supply while the remaining 58% obtained water from rivers, wells, springs and ponds. From the households of the children with visible goitre, 63.8% were supplied with treated tap water, while only 20% of the households of the non-goitrous children had similar water supply.

Table 8 shows the matched case-control pairs with and without treated water supplies. The odd ratio was 5.3 with a 95% confidence limits of 3.5 to 8.04. Statistical test using McNemar's Chi-square showed a very significant (P<001) association between treated water supply and the occurrence of goitre .

Table 8: Treated water supply and risk of endemic goitre: matched analysis.

		Non-goitrous	
		Treated Water Used (n)	Treated water Not Used (n)
Goitrous	Treated water used	25	117
	Treated water not used	22	71
	Total	47	188

OR=5.3 X2=63.57 d.f=1 P<0.0001)

When the estimate of the relative risk of visible goitre associated with treated water supply was done ignoring the matched pairs in the analysis, the risk was 6.1 with a 95% confidence limits of 4.09 to 9.08. Chi-square test showed that this association was significant (p<0.001). Further analysis for the association between the use of treated water supply and visible goitre was done separately for each stratum of ethnic group (Table 9). Among the Sidama ethnic group, the estimated relative risk of visible goitre associated with treated water supply was 3.52 with a 95% confidence limits of 2.09 to 5.95. For the non-Sidama group, the estimate of the relative risk was 4.20 with a 95% confidence limits of 1.10 to 16.01. A weighted average estimate of the relative risk (Mantel-Haenszel weighted odds ratio) was 3.60 with a 95% confidence limits of 2.29 to 5.66. Use of the appropriate Mantel-Haenszel chi-square showed that the association was significant (P<0.001).

Table 9: Treated water supply and risk of endemic goitre, stratified by ethnic groups

Ethnic Group	Water source	Goitrous (n)	Non-goitrous (n)	Total (n)
Sidama	Treated	84	10	94
	Untreated	12	6	18
	Total	96	16	112
Non-Sidama**	Treated	58	37	95
	Untreated	81	182	263
	Total	139	219	358

* OR=3.52 X^2=6.30 d.f=1 P=.012

** OR=4.20 X^2=26.82 d.f=1 P<.001

4.2.3.2. *Unprotected water supply*

The association between the presence of goitre and the use of unprotected water supplies was assumed. The matched odd ratio was 0.37 with 34 case control pairs in which only the case had used unprotected water compared to 91 in which only the control had used so (Table 10). when the matching was ignored, the estimate of the relative risk (odds ratio) was 0.35.

Treated water supply was considered as protected in the matched analysis as it was also a risk factor for endemic goitre. Thus, an estimate of the association between unprotected water supplies and goitre was calculated for treated and untreated water sources separately (Table 11). The Mantel-Haenszel weighed odds ratio was 1.1 with a 95% confidence limits of 0.66 to 1.85. There was no significant association (p=0.70) between unprotected water sources and visible goitre.

Table 10: Unprotected water sources and risk of endemic goitre: matched analysis.

		Non-goitrous	
		Unprotected Water Used (n)	protected Water Used (n)
	UnProtected water used	26	34
Goitrous	protected water used	91	84
	Total	118	117

OR=0.37 X2=25.99 d.f=1 P<0.001

Table 11: Unprotected water supplies and risk of endemic goitre,stratified by water treatment.

type of water	water source	Goitrous (n)	Non-goitrous (n)	Total (n)
Treated*	unprotected	0	0	0
	protected	142	47	189
	Total	142	47	189
Untreated**	Unprotected	60	117	177
	Protected	33	71	104
	Total	93	188	281

* X^2 and P values could not be calculated
** OR=1.1 X^2=0.14 d.f=1 P=0.70

4.2.4.. Fluorosis

Sixty percent of the children with visible goitre and 49.4% of the children without goitre had fluorosis. The distribution of the matched case-control pairs is presented in Table 12. In 67 case-control pairs only the cases had fluorosis while in 42 pairs only the controls had the same problem. The matched odd ratio was 1.6 with a 95% confidence limits of to 1.08 to 2.35. The significance of this association could not be determined accurately due to the small sample size.

Table 12: Fluorosis and risk of endemic goitre:matched analysis.

		Non-goitrous	
		With Fluorosis (n)	Without Fluorosis (n)
Goitrous	With Fluorosis	74	67
	Without Fluorosis	42	52
	Total	16	119

OR=1.6 X2=5.73 d.f=1 P<0.02

4.2.5. Nutritional Status (Height for Age)

The mean heights of the children with visible goitre and without goitre were 138.4 cm and 139.8 cm, respectively. Eighteen percent of the children with visible goitre were below -2SD height for age compared to 12.8% of the non-goitrous.

Table 13 shows the distribution of the matched case-control pairs who had their heights for age below -2SD and those above -2SD of the WHO standards in their observed heights for their ages at the time of the study. For simplicity, the z-score method was used. The odd ratio was 1.7 with a 95% confidence limits of 1.02 to 2.81. Due to the small sample size, the significance of the association could not also be determined for this variable, accurately.

Table 13: Height for age <-2SD and risk of endemic goitre: matched analysis.

		Non-goitrous	
		<-2SD (n)	>-2SD.H/A (n)
Goitrous	<-2SD.H/A	5	38
	>-2SD.H/A	22	170
	Total	27	208

OR=1.7 X^2=4.26 d.f=1 $p<0.05$

CHAPTER FIVE

DISCUSSION

5. 1 Prevalence of goitre in school children in relation to iodine intake.

The results of this investigation suggest that endemic goitre is a very serious public health problem in the study area, although the extent of physical and mental handicap related to it was not assessed. The high prevalence of goitre (61.7%) as shown in Table 1, however, is not surprising since other surveys conducted in the country have shown prevalence rates as high as 72% total goitre and 48% visible goitre (ENI, 1980). The prevalence of goitre in females is higher than in males. The peak total prevalence for both males and females is in the 6-8 age group while the peak visible goitre prevalence for males and females is in the 12-14 and 15-17 age groups, respectively. This sex and age distribution of goitre among school children in the study area is also similar to the earlier studies in different regions of the country (ENI, 1980).

The striking observation of the prevalence survey was the difference in the prevalence rates of endemic goitre among the six study schools despite their apparently similar environmental characteristics and their geographic proximity to each other (Figure 1).

It is generally accepted that iodine deficiency is the dominant factor in the development of endemic goitre (Stanbury, 1987). However, a situation in which no goitre was evident despite severe dietary iodine deficiency has been reported (Delange et al., 1968). On the other hand, studies conducted in Northern Virginia (Vought et al., 1967) and Ceylon (Mahadeva et al., 1968) have also indicated that high prevalence of goitre can occur where there is adequate iodine intake by the population. As indicated in Section 4.2.1., the mean values for urinary iodine concentration levels of the children with visible goitre and without goitre were the same. This observation is in agreement with previous studies in the Andean region of Colombia (Gaitan et al., 1978), the island of Idjwi (Delange et al., 1968) the endemic areas of Central Greece (Malamos et al., 1966) and Eastern Kentucky (London et al., 1965). This would suggest that the iodine intakes of the two groups were the same. Thus, the first hypothesis in this study which stated that "The iodine intake, as measured by urinary iodine excretion, of children with visible goitre is significantly lower than that of non goitrous children" is therefore rejected.

Table 14 shows the scheme recommended by UNICEF, WHO and ICCIDD (1990) for classification of goitre endemicity into three stages of severity: mild, moderate and severe with typical values for their median urinary iodine concentration levels (Dunn and Vandr-Haar, 1990).

According to these standards, severe iodine deficiency is characterized by urinary iodine excretion level of <2 ug. The high prevalence of endemic goitre in the study area is not consistent with these standards given that more than 80% of the urine samples showed iodine concentration levels above 10 μg/dl (Table 2). This observation showed that dietary iodine deficiency can not explain endemic goitre in the study area and that factors other than nutritional iodine deficiency might be responsible for differences in goitre prevalence. This is further confirmed by the observation that there is marked difference in goitre prevalence among the school children from different schools located in the same community.

Table 14: Scheme for classification of Goitre stages of severity with typical values for their urinary iodine levels

Stage	Typical goitre prevalence %	Median urinary iodine ugl/dl
Mild	10-30	3.5-5.0
Moderate	20-50	2.0-3.5
Severe	30-100	<2.0

Source: Dunn, J.T. and Vander-Haar (1990). A practical guide to the correction of iodine deficiency. ICCIDD technical manual No. 3, p. 19.

5. Factors associated with endemic goitre in school children.

5.1 Types of foodstuffs

In the matched pair analysis, the association of daily consumption of teff with the presence of visible goitre in the study children was very striking. A child who consumed teff everyday was 19.5 times more likely to have visible goitre compared to a child who did not do so.

As it is evident from the fact that the unmatched estimate of the relative risk (odds ratio = 12.5) calculated from the matched pair analysis (Table 4) was appreciably different from that of the matched. Sex and age (the matching variables) were therefore, in fact confounders of the association between daily consumption of teff and visible goitre. It is clear that ethnicity is also a confounder in the association because when the unmatched data was stratified by ethnic groups (Table 5) to control the confounding effect the odds ratio was reduced to 5.5.

The magnitude of the underestimating the effect that may be introduced by analyzing matched data as if they were unmatched relates to the degree of confounding by matching factors. Thus, the effect of the matching variables must be taken into account in the stratified analysis to provide a valid estimate of the association between every day consumption of teff and visible goitre. Therefore, a valid estimate of the relative risk would be 12.5 which is the sum of the magnitude of the underestimate (introduced by analyzing matched data as if they were unmatched) and the estimate of the relative risk from the stratified analysis

The observation pointed strongly to the presence of a goitrogenic agent in teff. Unfortunately, teff (indigenous only to Ethiopia), to the knowledge of the writer, has never been investigated for goitrogens. However, studies conducted in Darfur Province in Sudan have indicated that millet, which is related to teff, contains a goitrogenic agent (Osman, 1981). The same author refers studies conducted in Cameroon, Nigeria and India that incriminated millet as a possible contributory factor to the goitre endemicity.

Previous studies conducted in Ethiopia have not indicated any association between teff consumption and endemic goitre. However, it has been reported that areas with high altitude appear to be more affected than those of low altitudes (ENI, 1980). The staple food of most Ethiopians living in highland areas is mainly made from teff, suggesting the possibility of involvement of teff in the high endemicity.

In case of sugarcane, the relative risk estimates from the matched and unmatched data had been similar (Section 4.2.2.2.). There was a confounding effect of the association between consumption of sugarcane more than two days per week and visible goitre by ethnic group as shown in Table 7. Thus, instead of estimating 4.4 as the odds ratio relating consumption of sugarcane more than two times per week to visible goitre, it was estimated to be 2.92 after removing the confounding effect of ethnic group .

In summary, these results clearly indicate that high frequency of teff consumption is strongly associated with the high endemicity of goitre in the study area. The findings are also suggestive of the possibility that high sugarcane consumption is a contributory factor to the high endemicity of goitre in the area. Therefore, the second hypothesis of this study which states that "Frequent consumption of certain common foods in the study area exposes children to a significantly higher risk of endemic goitre than those who do not consume or with low frequency of consumption of these foods" is accepted. It is, however, possible that the effect of these foods is a result of interaction with other factors.

5.2. Types of drinking water supplies

5.2.1 Treated public water supply

Matched pair analysis has shown that a child who was supplied with treated water was 5.3 times more likely to develop endemic goitre than the one who was supplied with untreated water (Table 8). On the other hand, the ethnic groups of the study children were highly related with the treated or untreated water supplies. Eighty-four percent of the non-Sidama ethnic group were supplied with treated water while only 26.5% of the Sidamas had the same supply. This difference could be explained by the fact that most of the non-Sidama population had settled in the area where the treated water supply line passes unlike most Sidamas who stayed a few kilometres away from it. Thus, the estimate of the association between the use of treated water supply and visible goitre was adjusted for ethnicity and the unconfounded estimate of the relative risk was 3.6. This was still significant ($p<0.001$) as shown in Table 9. In the stratified analysis, if the overestimate of the odds ratio brought about by the conversion of the matched data into unmatched data (Section 4.2.3.1.) is taken into account, the estimate of the relative risk would be 2.8.

Contrary to this finding, a study conducted in Western Colombia to determine the effect of water treatment on goitre prevalence in the school population of Ginebra and

Guacari, indicated that treatment of water with chlorine reduces the rate of endemic goitre (Gaitan, 1973).

Chlorine was also used in the treatment of water in the present study area. Both chlorine and iodine are halogens but chlorine is more reactive than iodine. It has been postulated that relationship between water treated with chlorine and endemic goitre could be due to the possibility that chlorine is competitively taken up by the thyroid gland. This inhibits the iodine transport mechanism and reduces its availability as substrate for thyroid hormone formation (Editorial, 1982). The result in this study would seem to support the postulation. The hypothesis in this work which stated, that "Children who get treated drinking water supply have a significantly higher risk of endemic goitre than those who get untreated water" would therefore be accepted.

5.2.2 Unprotected water supplies

That bacterial pollution of water is associated to endemic goitre was known since the turn of the century (Malamos et al., 1971; Gaitan et al., 1980 and Ramalingaswami et al., 1961). However, the results obtained in the present investigation seem to indirectly contradict these observations.

In the matched analysis given in Table 10 the estimate of the relative risk (odds ratio =0.34), indicates that there is a protective effect of unprotected water sources on risk to goitre. In this analysis, the children who got treated water supply were herein counted as getting protected water supply. Thus, the data was analyzed only for children who got untreated water and the odds ratio increased to 1.1 (Table 11), indicating the confounding of the association between unprotected water and visible goitre by treated water supply. In other words, the observed protective effect of unprotected water sources on risk of goitre was the confounding impact of treated water sources in the analysis.

A possible explanation for the low estimate of the relative risk might be similarity of the protected and unprotected water sources in the study area in terms of the degree of bacterial pollution.

The sample size considered in this investigation was too small to detect a statistically significant association between the unprotected water sources and visible goitre in the study children. This is because, the sample size was determined only to detect the major risk factors which contributed more than a two fold increase in the occurrence of visible goitre. The observations made in this study, however, strongly indicated that the estimate of the relative risk of visible goitre associated with the use of unprotected water sources was low in the area. The results suggest that the hypothesis in this study which stated that, "Children who get their drinking water from unprotected water sources have a significantly higher risk of endemic goitre than those who get their drinking water from protected sources" may not be acceptable. However, it is difficult to conclusively reject the hypothesis due to the small sample size.

2.4. Fluorosis

The odd ratio of fluorosis associated with endemic goitre was lower than the anticipated value used in the sample size determination. The result shows that the occurrence of visible goitre was higher in children with fluorosis than those without the problem (Table 12). However, the real odd ratio and the significance of the association could not be determined due to the small sample size. Thus, the hypothesis which stated that, "Children who have fluorosis are at a significantly higher risk of endemic goitre than those who do not have this nutritional problem" could neither be accepted nor rejected accurately.

A relationship between goitre and fluorosis was suggested in Kenya based on an observation that goitre endemic areas coincide with areas where the prevalence of fluorosis is high (Editorial, 1982). A correlation between goitre prevalence and fluoride content of drinking water has also been observed in the Himalayan villages (Day, 1972).

Fluoride, chlorine, iodine and bromine are all halogens. Fluorine is the most reactive and iodine the least reactive of the halaides given (Editorial, 1982). The higher odd ratio of goitre in children who used chlorine treated water than those who had fluorosis suggested that the concentration of chlorine in water might be markedly higher than that of fluorine. Even though fluorine is more reactive than chlorine, the abundance of the later in drinking water might have given it a higher chance to interfere with the absorption of iodine by the thyroid than fluorine. Representative figures of fluorine and chlorine concentrations in drinking water of the study area should be obtained to substantiate this hypothesis.

5.2.5. Nutritional Status (Height for Age)

Since it is an established fact that one of the disorders associated with endemic goitre is stunted growth (Hershman et al, 1986), only the parameter height for age was used as an indicator of the nutritional status of the study children.

Previous studies have reported conflicting results about the correlation between endemic goitre and stunting (Bautista et al., 1977; Barazelatt et al., 1969; Koutras, 1973). The findings of the present work (Table 13) indicate that the children with visible goitre had a higher proportion of stunting than the non-goitrous ones. However, since the estimate of the relative risk (odds ratio) was below two (minimum detectable odds ratio), a higher sample size would have been required to detect whether stunting is significantly associated with the occurrence of endemic goitre in the study population.

This means that the last hypothesis of this study which stated that, "Children who are stunted (below -2S.D height for age) have a significantly higher risk of endemic goitre than those who have normal growth (above -2 S.D height for age)" could neither be rejected nor accepted accurately.

CHAPTER SIX

6.1 CONCLUSION AND RECOMMENDATIONS

6.1.1 Conclusion

Iodine deficiency is most probably not the main cause of the high prevalence of goitre in the Sidama region of sourthen Ethiopia and it does not appear to account for the different clinical conditions of the goitrous and non-goitrous children of the study area. There is evidence that the chronic consumption of teff is a major factor associated with the occurrence of visible goitre in the study children. The results strongly suggested that teff may contain a goitrogenic factor. Frequent consumption of sugarcane and use of chlorine treated water supply also appeared to be contributory factors for the high prevalence of goitre in the study of area.

The real magnitude and significance of the association of visible goitre with retarded growth (< -2SD height for age) and fluorosis in the study children can not be established, because the estimate of the relative risks (odds ratio) for the two factors were below the cut off point that the sample size of this study could detect.

In summary, the results suggest that the difference between the goitrous and non-goitrous children of the area is most probably due to the interplay of many factors including frequent teff and sugarcane consumption and the use of chlorinated water supply.

6.1.2. <u>Recommendations</u>

It is generally accepted that goitre and its associated disorders can be prevented by correction of iodine deficiency. In addition to correction of iodine deficiency by supplementation of the micronutrient, other measures which include the following should be considered.

1. Further studies are needed to determine whether there are goitrogenic factors in teff (Eragrositis abyssinica), and if so, identify them.
2. If the goitrogenic factor is identified, attempts should be made to develop teff varieties with low goitrogenic substance. Investigation should also be done to remove or reduce the level of the goitrogenic substance by processing.
3. Concentration levels of chlorine and fluoride in drinking water sources in the study area should be determined in order to prevent the excessive intake of these elements.
4. Few additional detailed studies should be conducted in areas of Ethiopia with high prevalence of goitre to further evaluate and confirm the observations of this work.

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Appendix 1

Procedure for the Preparation of Solutions used for measuring iodine in urine.

1. Chloric acid solution - In a 2000 ml Erlenmeyer flask dissolve 500g $KClO_3$ in 910 ml H_2O: heat until goes into solution. Then add 375 ml $HClO_3$ (perchloric acid, 70%) slowly (about 15 ml/minute) with constant stirring. Store in freezer overnight. Next day filter with filter paper (Watman # 1 or similar product), preferably on Buchner funnel. Volume of filtrate is approximately 850 ml. Store in refrigerator.

2. Arsenious acid solution - In a 2000 ml Erlenmeyer flask, place 10g AS_2O3 and 50g NaCl, then add 400 ml 5 N H_2SO_4 (made by slowly adding one part concentrated (36 N) H_2SO_4 to 6.2 parts deionized water (careful - generates heat!]). Add water to about 1 L, heat gently to dissolve, cool to room temperature, dilute with water to 2 L, filter, store in dark bottle, away from light, at room temperature. Stable for months.

3. Ceric ammonium sulfate solution - Dissolve 24g ceric ammonium sulfate in 1 L 3.5 N H_2SO_4 (made by slowly adding one part concentrated (36 N) H_2SO_4 TO 9.3 parts

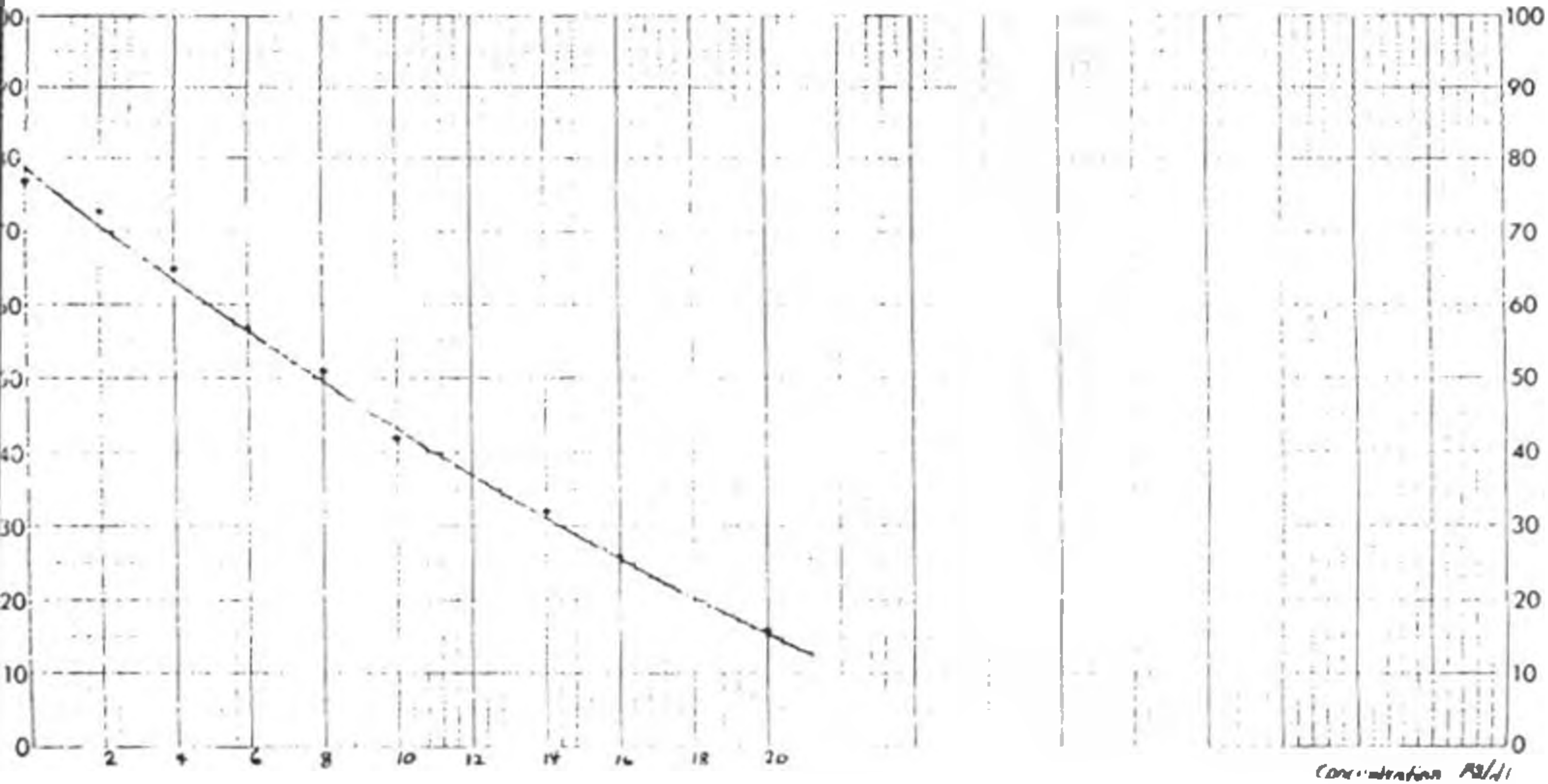
deionized water [careful - generates heat!]). Store in dark bottle away from light at room temperature. Stable for months.

4. Standard iodine solution, 1 µg iodine per ml - Dissolve 0.168 mg KIO_3 in deionized water to a final volume of 100 ml. It is frequently convenient to make a more concentrated solution, e.g. 10 or 100 mg/ml, and then dilute to 1 µg/ml. 1.68 mg KIO_3 contains 1.0 mg iodine. Store in dark bottle, stable for many months. (KIO_3 is usually preferred over KI for a standard because it is more stable, but KI has been used by some laboratories without apparent problems.

Standard curves for each assay can either be prepared fresh each time by appropriate dilutions of the 1 µg/ml solution of KIO_3, or one can make individual stock solutions of the desired iodine concentrations. The following are useful standards: 2, 4, 6, 8, 10, 15, 20 µg/dl.

Appendix 2

A standard curve: iodine concentration of each standard iodine solution against its spectrophotometer reading.



APPENDIX 3

Distribution of study children by frequency of consumption of commonly consumed foods and by study groups (n = 470)

Type of food	Study group	Proportion of children with the following days of consumption per month			
		0	1 - 8	9 - 16	17 - 30
Teff[a]	Goitrous	14.9[g]	33.6	16.1	35.3
	Non-goitrous	37.4	52	6.4	4.3
Enset[b]	Goitrous	15.3	49.8	28.1	6.8
	Non-goitrous	.9	37	51.5	10.6
Maize[c]	Goitrous	21.3	21.7	29.3	27.7
	Non-goitrous	3	21.7	28.9	46.4
Cabbage[d]	Goitrous	3.8	6.3	17.5	15.8
	Non-goitrous	1.3	43	31.5	24.2
Milk[e]	Goitrous	26.8	37	17	19.1
	Non-goitrous	3.4	41.3	18.3	37
Sugarcane[f]	Goitrous	3.8	74.1	16.6	5.5
	Non-Goitrous	2.6	91.1	2.5	3.8

[g] All figures are in percentages

[a] χ^2 = 100.6 D.f = 5 $P < .001$

[b] χ^2 = 62.0 D.f = 6 $P < .001$

[c] χ^2 = 48.3 D.f = 6 $P < .001$

[d] χ^2 = 39.9 D.f = 6 $P < .001$

[e] χ^2 = 66.2 D.f = 8 $P < .001$

[f] χ^2 = 39.2 D.f = 7 $P < .001$

APPENDIX A

Distribution of study children by frequency of consumption of commonly consumed foods and by ethnic groups
(n - 470)

Type of food	Ethnic group	Proportion of children with the following days of consumption per month			
		0	1 - 8	9 - 16	17 - 30
Teff[a]	Sidama	33.0[d]	53.3	7.5	6.1
	Non-Sidama	4.5	8.9	23.2	63.4
Enset[b]	Sidama	1.4	38.8	48.3	11.5
	Non-Sidama	29.5	58.0	12.5	0.0
Maize[c]	Sidama	3.9	19.5	31.8	44.7
	Non-Sidama	38.4	28.6	20.5	12.5
Cabbage[d]	Sidama	2.5	50.9	24.3	22.4
	Non-Sidama	2.7	59.8	25.1	12.5
Milk[e]	Sidama	6.4	41.1	20.4	32.2
	Non-Sidama	42.9	33.0	8.9	15.2
Sugarcane[f]	Sidama	4.2	72.3	5.4	4.7
	Non-Sidama	0	72.7	23.2	4.5

[d] All figures are in percentages

[a] χ^2 = 230.3 D.f = 5 P < 001

[b] χ^2 = 140.1 D.f = 6 P < 001

[c] χ^2 = 115.3 D.f = 6 P < 001

[d] χ^2 = 20.4 D.f = 6 P < 002

[e] χ^2 = 97.3 D.f = 8 P < 001

[f] χ^2 = 47.3 D.f = 7 P < 001

APPENDIX 5

Distribution of the study children by ethnic groups

n = 470

School	Children		Total
	Without goitre	With visible goitre	
Sidama	219 (61.2)[#]	139 (38.8)	358 (76.2)
Amhara	8 (3.4)	54 (23.0)	62 (13.2)
Wolaita	5 (2.1)	21 (8.9)	26 (5.5)
Oromo	1 (0.43)	16 (6.8)	17 (3.6)
Gurage	2 (0.85)	5 (2.1)	7 (1.5)
Total	235 (50)	235 (50)	470 (100)

[#] Figures in parenthesis are percentages.

APPENDIX 6

Ddstribution of the study Children by Water Source

Water Source	Study Children		
	Without Goitre	With Visible Goitre	Total
Tap	47 (23.9)*	150 (76.2)	197 (41.9)
River	48 (67.6)	23 (32.4)	71 (15.1)
Stream	15 (71.4)	6 (28.6)	21 (4.5)
Spring	80 (70.8)	33 (29.2)	113 (24.0)
Well	14 (42.4)	19 (57.6)	33 (7.0)
Pond	31 (88.6)	4 (11.4)	35 (7.4)
Total	235	235	470

* Figures in parenthesis are percentages

Appendix 7

Questionnaire

Part 1.- Identification:

Region __________ District _______ Village _______

Town __________________ House No _____________

Name of Interviewer ______________________________

Name of Respondent ______________________________

Case Pair No _____________ Control Pair No __________

School ______________ Grade and Section ____________

Part 2 - Demography

1. Name of Child _____________________

   Sex of child 1. Male | | 2. Female | |

2. Respondent child relationship.

   1. Mother 3. Care taker

   2. Father 4. Other specify __________

3. Name of the head of the housedhold ________________

4. Occupation of the head of the household.

   0 = Not applicable

   1.= Farmer 3. Government employee 4. Trader.

   2. Father. 5. Handcrafts man 6 other (specify)

   ____

5. Ethnic group __________________________

6. Estimated total income of the household (write actual amount per annum) ____________ Ethiopia birr per year.

7. Number of household members __________________

8. Date of the birth of the child. ______________

   Year ____________ Month ___________________

   Date verified 1. Yes 2. No.

   If No, estimated age of the child ___________

9. Birth order of the child ___________________

10. Duration of child's stay in the area

    1. < 1 Year 3. 2-5 Years.

    2. 1-2 Years 4. > 5 Years.

Part 3- Clinical examination

1. Child's goitre grade ____________
2. Does the child have the following signs of malnutration?.

   1. Yes 2. No.

a. Vit. A deficiency b Fluorosis

- Conjuctival xerosis
- Bitot's spot
- Corneal Xerosis
- Keratomalacia
- Mottaled enamel

Part 4- Anthropometric measurement

	OBS1	OBS2	Average
Height	_____	_____	_____

Part 5- Drinking water

1. Source of drinking water

1. Tap 3.Stream 5. Well
2. River 4. Spring 6 Other ________

2. Source of drinking water 1. Treatecd 2. Untreated
3. Source of drinking water 1. protected 2. Unprotected
4. Local name (if any) and the location of the water source____
5. How long have you used the present water source?
1. < 1 Year 3. 3-4 Years
2. 1-2 Years 4. > 5 Years

Part 6.- Laboratory results.

1. Code name of urine sample ________________
2. Urinary iodine excretion ________________

Part 7. Food Frequency questionnare for commonly consumed foods in the study community

1. Does the child eat "Enset (worke) 1. Yes 2 No.
1.1 If so how often? 1. Every day 2.______/week 3._____/month
2. Does the child eat "Teff" 1. Yes 2. No.
2.1 If so how often? 1. Every day 2.____/week 3. ____/month
3. Does the child eat cabbage? 1. Yes 2. No.
3.1 If so how often 1. Every day 2._____/week 3._____/month
4. Does the child get milk. 1. Yes 2. No
4.1 If so how often 1. Every day 2.____/week 3._____/month
5. Does the child eat sugar cane? 1. Yes 2. No.
5.1 If so how often. 1 Every day 2.____/week 3.____/month
6. Are there other foods that the child eats usually?
1. Yes 2. No.
6.1 If yes, what are they and how often

________ ____________ _______________ ___________

_________ ___________ _____________ ______________