University of Khartoum  
Faculty of Pharmacy  
Department of Pharmacology  

Prevalence of Iodine Deficiency in school children in selected sites in the White Nile North of Kosti town and Estimation of Iodine in Local Water and Salt Used  

By  
Ahmed Salah Rashid  
B. Pharm, M. Pharm (University of Khartoum)  

A thesis submitted in fulfillment of the requirement for the Ph.D Degree in pharmacy  

Supervisor:  
Professor El Daw Mukhtar  

Co-supervisor:  
Dr. Sania A. I. Shaddad  

2005
DEDICATION

TO THE SOUL OF MY MOTHER
ACKNOWLEDGMENTS

First and foremost I am thankful to Almighty Allah.

I am indebted to Professor Eldaw Mukhtar my supervisor, for his continuous support, encouragement and guidance throughout the course of the work.

I am grateful to Dr. Sannia A. I. Shaddad my co-supervisor who contributed her time, knowledge and efforts to help me to conduct this work.

I am greatly obligated to Dr. Mohammed Sedig (Sudan Atomic Energy Commission) for allowing me to carry out part of this work in his laboratory and for his help and valuable advice during this work. I also extend my gratitude to Department of pharmacology and professor Kamal Eldin Eltyeb the head of department of chemistry- faculty of Pharmacy U.of K. and all staff of the two departments for laying their facilities at my disposal. I am grateful to Khartoum State Water Corporation especially the central laboratory for carrying out part of the analysis in their laboratory.

Finally, I am indebted to my wife, my parents, my brothers and my sisters who offered endless devotion, continuous support and encouragement throughout this work.
Abstract

Iodine deficiency disorders (IDD) constitute one of the major health problems of the world. In the Sudan during the last 50 years a number of reports appeared about the prevalence of goiter in different region in Sudan especially in Darfur (in the West), Kosti (in the centre) and Khartoum (the capital of Sudan). In this study we concentrated on the central area around the White Nile which lies between Kosti and Khartoum. Four cities around the White Nile on the eastern bank lie Rabak and Jabal Awlia and on the western bank lie Kosti and Elfetihab. The aim of the study was to assess the prevalence of ID in schoolchildren aged 6-18 years and to estimate the iodine content in local water and iodized salt. Stratified random urine samples were collected from two hundred ninety one (136 male and 155 female) schoolchildren and forty one blood samples (13 male and 28 female) during the period from February 2003 to March 2004. Eight samples of water from each of the following: White Nile-Kosti, White Nile-RabaK, White Nile-Elfetihab, Blue Nile-Sennar, Nile River-Dongola, tap water-Kosti, Aasel well-Kosti, Umukkaz well-Kosti, tap water-Rabak, Asalya Canal, Albank Alagary tank-Elfetihab, Wadalbasheir tank-Elfetihab and Abuseid tank-Elfetihab. Eighteen iodized salt samples were collected from the market, twelve from salt packaged in high density polyethylene containers and six from salt packaged in low density polyethylene containers. The urine samples and water samples were analyzed spectrophotometrically by Sandell-
Kolothoff reaction the method recommended by WHO. The water was reanalyzed by Khartoum State Water Corporation- The Central Laboratories- for further insurance. Serum T₃ and T₄ concentrations were measured by Radioimmunoassay technique. Thyroid stimulating hormone (TSH) was measured by immunoradiometric assay. The salt samples were analyzed by titration with potassium iodate. The analysis of urine shows that the median urinary iodine excretion (UIE) in Kosti, Rabak, Jabal Awlia and Elfetihab were 0.54 µg/dl, 5.66 µg/dl, 1.1 µg/dl, and 2.60 µg/dl respectively. 52.9% of the female and 56.6% of the male UIE was less than 2 µg/dl, while 11.8% of the male and 20.6% of the female UIE was above 10 µg/dl. Generally the median UIE for the total samples was 1.3 µg/dl which means sever iodine deficiency in the study area. The mean serum T₃ and T₄ found to be in the low normal level. The mean ± SD serum T₃ was 0.99 ± 0.32 nmol/L. It was higher in female than in male. The mean ± SD serum T₄ was 95.80 ± 24.06 nmol/L and also it was higher in the female. The serum TSH was on the high normal level. The mean serum TSH ± SD was 2.06 ± 0.90 mU/L but it was lower in the female than that in the male. Iodine in water samples from the White Nile was low and decline gradually from Kosti to Elfetihab. The iodine in the White Nile was higher than that in the Blue Nile which it self was higher than the iodine in the River Nile. The water iodine content in the tap water and wells samples were low range from 3.5 µg/l to 0.3 µg/l. The iodized salt loses most of its iodine within twelve months. But the
decrease in the iodine concentration was dramatically in the high density polyethylene packaged salt.
ملخص الرسالة

يعتبر مرضاً قليل يدوم أحد أهم المشاكل الصحية في العالم. في منتصف العقد
الماضي صدر عدة تقارير توضح حجم انتشار مرضاً قليل يدوم تضخم الغدة الدرقية في مناطق
مختلفة من السودان خاصة في دارفور (في الغرب) و في كوشتي (في الوسط) وفي
الخرطوم (عاصمة السودان).

في هذه الدراسة تم التركيز على منطقة الوسط وخاصة حول مجرى النيل
الأبيض في المنطقة الممتدة بين كوشتي والخرطوم. أُخذت أربعة من خلال النيل الأبيض
هي ريك و جبل أولياء في جهة الشرق، وكوستي والفتحاب في جهة الغرب. الهدف من
هذه الدراسة تقاسّي مدى إنتشار مرضاً قليل يدوم بين طلبة المدارس في سن 6-18 سنة,
والتحديد نسبة اليدود في المياه المحلية وكذلك الملح المعالج باليدود. عشانها جمعت مانتان
وواحد و تسون عينة بول (136 من الأولاد و 155 من البنات) من طلبة المدارس،
و كذلك جمع واحد واردب عينة دم (13 من الأولاد و 28 من البنات) في الفترة من
فبراير 2003 حتى مارس 2004. جمع كذلك ثمانية عينات من الماء من كل من: مياه
النيل الأبيض-كوستي، مياه النيل الأبيض-ريك، مياه النيل الأبيض-الفتحاب، مياه النيل
الأزرق-سنار، مياه نهر النيل-دنقلا، مياه الشرب-كوستي، مياه بنر أعمل-كوستي، مياه
بنر أم عكاوس-كوستي، مياه الشرب-ريك، مياه ترعة عمالية، مياه خزان البنك العقاري-
الفتحاب، مياه خزان رود البشير-الفتحاب، و مياه خزان أبو سعد-الفتحاب. ثمانية عشر
عينة ملح معالج باليدود جمعت من السوق اثنا عشرة عينة منها من الملح المعالج باليدود من
مادة البولي إيثيلين عالي الكثافة و ست عينات من النوع المعبأ ببكياس من مادة البولي
إيثيلين قليل الكثافة. عينات البول و عينات الماء حلست بواسطة جهاز مقياس الطيف
الضوئي تفاعل ساندل-كلوثوف وهي الطريقة المعتمدة من منظمة الصحة العالمية. الماء
أعيد تحليلة بواسطة المعمل الرئيسي باللهجة القومية لمياه ولاية الخرطوم للتأكد من
النتائج بصورة أفضل. أما تركيز هرمون ثلاثي بود ثيرونين والثيروكسيسين فقد قيس
إلى الطريقة التحليل الشعاعي المناعي. أما هرمون ممنه الدراية فقد قيمه بطريقة القياس
الشعاعي المناعي. الملح المعالج باليدود حلّ بالمعايرة مع أبودات البوتاسيوم. تحليل
البول بين أن متوسط إخراج اليوس في البول في كل من كوسنتي، ريك، جبل أولياء والفتاح كان 0.54 ميكروجرام/ديستر، 5.66 ميكروجرام/ديستر، 1.1 ميكروجرام/ديستر، و 2.60 ميكروجرام/ديستر على التوالي. 52.9% من البناط، و 56.6% من الأولاد كان معدل إخراج اليوس في البول لديهم أقل من 2 ميكروجرام/ديستر، بينما 11.8% من الأولاد و 20.6% من البناط كان معدل إخراجهم من اليوس في البول أعلى من 10 ميكروجرام/ديستر. بصورة عامة متوسط إخراج اليوس في البول من مجموع العينات كان 1.3 ميكروجرام/ديستر وهذا يعني وجود نقص حاد في اليوس في هذه المنطقة. متوسط تركيز هرمون ثلاثي يود الثيرونين والهرمون الثلاثي يود في البلازما كان أدنى المعدل الطبيعي. المتوسط ± معدل الانحراف لثلاثي يود الثيرونين هو 0.99 ± 0.32 نانومول/لتر. وقد كان في البناط أعلى منه في الأولاد. متوسط ± معدل انحراف تركيز الثيرونتين في البلازما كان 95.8 ± 24.06 نانومول/لتر، وكان أيضاً أعلى في البناط. تركيز هرمون منبه الدرقي في البلازما كان في أعلى المعدل الطبيعي. متوسط تركيز ± معدل الانحراف لهرمون منبه الدرقي في البلازما كان 2.06 ± 0.90 مل وحده/لتر، لكنه كان في البناط أعلى منه في الأولاد. تركيز اليوس في عينات المياه المأخوذ من مياه النيل الأبيض كان قليلا وقد تناقص تدريجيا من كوسنتي إلى الفتيحاب. تركيز اليوس في حبوب المياه الأبيض كان أعلى منه في قليا في مياه النيل الأزرق والذي كان بدوره أعلى من مياه نهر النيل. اليوس في عينات مياه البحر والأبار كان منخفضاً وتراوح ما بين 3.5 ميكروجرام/لتر إلى 0.3 ميكروجرام/لتر. الملحق المعالج باليوس فقد معظم اليوس خلال أثني عشر شهراً، لكن النقص في تركيز اليوس كان سريعاً في الملح المعبا بأكياس البولي إيثيلين عالي الكثافة.
# TABLE OF CONTENTS

* Dedication I
* Acknowledgment ii
* Abstract (English) iii
* Abstract (Arabic) vi
* Table of contents viii
* List of tables x
* List of figures xii

1 Introduction 1
1.1 Thyroid gland 1
1.2 Action of thyroid hormones 3
1.3 Thyroid hormone metabolism 4
1.3.a Thyroid hormone synthesis 4
1.3.b Thyroid hormone degradation 6
1.4 Thyroid disorders 7
1.5 Goitre (endemic goitre) 8
1.6 Goitrogens 12
1.7 Iodine deficiency disorder (IDD) 15
1.8 Iodine deficiency in Sudan 23
1.9 Strategies for the prevention of IDD 24
1.10 Iodine 28
1.10.1 Iodine distribution 28
1.10.2 Iodine content of food 30
1.10.3 Chemical forms of iodine 30
1.10.4 Iodine usage 31
1.10.5 Importance of iodine for human 31
1.10.6 Effect of excess iodide 32
1.10.7 Iodine measurement 33
1.10..7.a Direct measurement of iodine intake 33
1.10.7.b Indirect measurement of iodine intake 34
       Urinary iodine 34
1.11 Aim of the study 36
2 Material and methods 38
2-1 Study area 38
2-2 The study population 38
2-3 Sampling of urine 41
2-4 The methods for measuring iodine in urine 41
2-5 Sampling of water 44
2-6 The method for measuring iodine in water 44
2-7 Sampling of blood 44
2-8 The method for measuring the serum T₃, T₄ and TSH 45
2-9 Sampling of salt 46
2-10 The method for measuring iodine in salt 47
2.11 Statistical analysis 48
3 The results 50
3.1 The results of urinary iodine excretion 50
3.2 The result of water analysis 73
3.3 The results of serum hormones analysis 73
3.4 The results of iodized salt analysis 82
4 The discussion 88
5 Conclusion and Recommendation 97
   Conclusion 97
   Recommendation 98
6 The references 101
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Drug affecting thyroid function</td>
<td>9</td>
</tr>
<tr>
<td>1.2</td>
<td>The relationship between iodine nutrition and urinary iodine concentration</td>
<td>35</td>
</tr>
<tr>
<td>2.1</td>
<td>Distribution of the collected urine sample</td>
<td>39</td>
</tr>
<tr>
<td>3.1</td>
<td>Urinary iodine excretion $\mu$g/dl in Kosti</td>
<td>53</td>
</tr>
<tr>
<td>3.2</td>
<td>Frequency of median urinary iodine excretion in Kosti</td>
<td>54</td>
</tr>
<tr>
<td>3.3</td>
<td>Urinary iodine excretion $\mu$g/dl in Rabak</td>
<td>56</td>
</tr>
<tr>
<td>3.4</td>
<td>Frequency of median urinary iodine excretion in Rabak</td>
<td>57</td>
</tr>
<tr>
<td>3.5</td>
<td>Urinary iodine excretion $\mu$g/dl in Jabal Awlia</td>
<td>59</td>
</tr>
<tr>
<td>3.6</td>
<td>Frequency of median urinary iodine excretion in Jabal Awlia</td>
<td>60</td>
</tr>
<tr>
<td>3.7</td>
<td>Urinary iodine excretion $\mu$g/dl in Elfitaihab</td>
<td>62</td>
</tr>
<tr>
<td>3.8</td>
<td>Frequency of median urinary iodine excretion in Elfitaihab</td>
<td>63</td>
</tr>
<tr>
<td>3.9</td>
<td>Urinary iodine excretion $\mu$g/dl in the four areas around the White Nile</td>
<td>66</td>
</tr>
<tr>
<td>3.10</td>
<td>Urinary iodine excretion $\mu$g/dl in the four areas around the White Nile in male and female</td>
<td>67</td>
</tr>
<tr>
<td>3.11</td>
<td>Urinary iodine excretion $\mu$g/dl in the four areas around the White Nile</td>
<td>69</td>
</tr>
<tr>
<td>3.12</td>
<td>Frequency of median urinary iodine excretion in all the study area</td>
<td>70</td>
</tr>
<tr>
<td>3.13</td>
<td>Frequency of median urinary iodine excretion in the four study areas</td>
<td>72</td>
</tr>
<tr>
<td>3.14</td>
<td>Water iodine content $\mu$g/l from different sites in the White Nile, Blue Nile and Nile River</td>
<td>75</td>
</tr>
<tr>
<td>3.15</td>
<td>Drinking water iodine content $\mu$g/l from different sites in the study area</td>
<td>78</td>
</tr>
<tr>
<td>Section</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>3.16</td>
<td>The concentration of thyroid hormones (T3, T4) and TSH in subjects from the study area</td>
<td>80</td>
</tr>
<tr>
<td>3.17</td>
<td>The effect of storage on the high density polyethylene packaging iodized salt</td>
<td>83</td>
</tr>
<tr>
<td>3.18</td>
<td>The effect of storage on the high density polyethylene packaging iodized salt without opening for 6 months</td>
<td>84</td>
</tr>
<tr>
<td>3.19</td>
<td>The effect of storage on the low density polyethylene packaging iodized salt</td>
<td>85</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

1.1 Algorithm for interpreting thyroid function tests
1.2 Map showing world wide distribution of iodine deficiency disorders (IDD)
1.3 Myxedematous endemic cretinism
1.4 A dwarfed cretin women
1.5 Three women with typical endemic goiter
1.6 A mother and child: the mother has a large goiter and the effect is cretinism in the child
2.1 Map of Sudan showing the White Nile, Blue Nile and the Nile River and the study area
3.1 Median urinary iodine excretion µg/dl in Kosti
3.2 Frequency of median urinary iodine excretion in Kosti
3.3 Median urinary iodine excretion µg/dl in Rabak
3.4 Frequency of median urinary iodine excretion in Rabak
3.5 Median urinary iodine excretion µg/dl in Jabal Awlia
3.6 Frequency of median urinary iodine excretion in Gabal Awlia
3.7 Median Urinary iodine excretion µg/dl in Elfetihab
3.8 Frequency of median urinary iodine excretion in Elfetihab
3.9 Median urinary iodine excretion µg/dl in the four areas around the White Nile
3.10 Median urinary iodine excretion µg/dl in the four areas around the White Nile in male and female
3.11 Median urinary iodine excretion µg/dl in the four areas around the White Nile 66
3.12 Frequency of median urinary iodine excretion in all the study area 68
3.13 Water iodine content µg/l from different sites in the White Nile, Blue Nile and Nile River 73
3.14 Water iodine content µg/l from different sites in the White Nile 74
3.15 Drinking water iodine content µg/l from different sites in the study area 76
3.16 The concentration of thyroid hormones T₃ in male & female in subjects from the study area 77
3.17 The concentration of thyroid hormones T₄ in male & female in subjects from the study area 78
3.18 The concentration of thyroid stimulating hormones TSH in male & female in subjects from the study area 78
3.19 The effect of storage on the high density polyethylene packaging iodized salt 80
3.20 The effect of storage on the high density polyethylene packaging iodized salt without opening for 6 months 81
3.21 The effect of storage on the low density polyethylene packaging iodized salt 82
3.22 The effect different packaging types on the iodized salt 83
### Abbreviation list

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIT</td>
<td>Diiodotyrosine</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>HDPE</td>
<td>High density polyethylene</td>
</tr>
<tr>
<td>ICCIDD</td>
<td>International Council for Control of Iodine Deficiency Disorders</td>
</tr>
<tr>
<td>IDD</td>
<td>Iodine Deficiency Disorders</td>
</tr>
<tr>
<td>IRMA</td>
<td>Immunoradiometric assay</td>
</tr>
<tr>
<td>LDPE</td>
<td>Low density polyethylene</td>
</tr>
<tr>
<td>MIT</td>
<td>Monoiodotyrosine</td>
</tr>
<tr>
<td>ppm</td>
<td>Part per million</td>
</tr>
<tr>
<td>RIA</td>
<td>Radioimmunoassay</td>
</tr>
<tr>
<td>rT₃</td>
<td>Reverse triiodothyronin</td>
</tr>
<tr>
<td>T₃</td>
<td>Triiodothyronin</td>
</tr>
<tr>
<td>T₄</td>
<td>Thyroxine</td>
</tr>
<tr>
<td>TPO</td>
<td>Thyroid peroxidase</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid stimulating hormone</td>
</tr>
<tr>
<td>UIE</td>
<td>Urinary iodine excretion</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Drug affecting thyroid function</td>
<td>9</td>
</tr>
<tr>
<td>1.2</td>
<td>The relationship between iodine nutrition and urinary iodine concentration.</td>
<td>35</td>
</tr>
<tr>
<td>2.1</td>
<td>Distribution of the collected urine sample</td>
<td>39</td>
</tr>
<tr>
<td>3.1</td>
<td>Median urinary iodine excretion µg/dl in Kosti</td>
<td>50</td>
</tr>
<tr>
<td>3.2</td>
<td>Frequency of distribution of urinary iodine excretion in Kosti</td>
<td>51</td>
</tr>
<tr>
<td>3.3</td>
<td>Median Urinary iodine excretion µg/dl in Rabak</td>
<td>53</td>
</tr>
</tbody>
</table>
3.4 Frequency of distribution of urinary iodine excretion in Rabak
3.5 Median Urinary iodine excretion μg/dl in Jabal Awlia
3.6 Frequency of distribution of urinary iodine excretion in Gabal Awlia.
3.7 Median Urinary iodine excretion μg/dl in El Fetibab
3.8 Frequency of distribution of urinary iodine excretion in El fitaihab.
3.9 Median Urinary iodine excretion μg/dl in the four areas around the White Nile
3.10 Median Urinary iodine excretion μg/dl in the four areas around the White Nile in male and female.
3.11 Median urinary iodine excretion μg/dl in the four areas around the White Nile.
3.12 Frequency of distribution of urinary iodine excretion in all the study area.
3.13 Frequency of distribution of urinary iodine excretion in the four study areas.
3.14 Water iodine content μg/dl from different sites in the White Nile, Blue Nile and Nile River.
3.15 Drinking water iodine content μg/dl from different sites in the study area.
3.16 The concentration of thyroid hormones (T3, T4) and TSH in subjects from the study area.
3.17 The effect of storage on the high density polyethylene packaging iodized salt.
3.18 The effect of storage on the high density polyethylene packaging iodized salt without opening for 6 months.
3.19 The effect of storage on the low density polyethylene packaging iodized salt.
INTRODUCTION

1.1 Thyroid gland

The thyroid is the largest endocrine gland in human, weighing about 20 g in an adult. It is frequently stated that the thyroid is so called because of its shield-shaped configuration (Nicholas 1986). In mammals the thyroid is derived from an evagination of the pharynx. The human thyroid gland develops from a midline thickening of the pharyngeal floor and paired caudal extension of the fourth pharyngobronchial pouches “lateral anlagen” (Fisher, 1992). These structures are discernible by 16-17 days of gestation. By 50 days, the median and lateral anlagen fuse and the buccal stalk ruptures. Then the thyroid gland migrates caudally to its definitive location in the anterior neck, aided in part by its relationship with developing cardiac structures. The gland approaches structural maturity by 17 weeks (Docain et al., 1992; Fisher, 1992).

The normal adult thyroid gland of the human is made of 2 lobes connected by a bridge of tissue, the thyroid isthmus, and there is sometimes a pyramidal lobe arising from isthmus in front of the larynx (Johnston, 1951; Romanes, 1993; Carlos et al., 1995). The structural unit of the thyroid is the follicle containing proteinaceous material colloid. The follicle consists of a simple epithelial sphere whose lumen contains colloid. A group of 20-40 follicles are bound
by connective tissue to form lobules; groups of lobules jointly form lobes (Docain et al., 1992; Ganong, 1995).

The thyroid is an extremely vascularized organ with an extensive blood and lymphatic capillary network surrounding the follicles (McMinn, 1984).

Endothelial cells of these capillaries are fenestrated, as in other endocrine glands. This fenestration facilitates the passage of the hormones into the blood capillaries (Carlos et al., 1995).

The thyroid function is to synthesize the hormones thyroxine (T₄) and triiodothyronin (T₃), which stimulate the rate of metabolism (Astwood; 1951; Nihei et al., 1971; Nunez and Gershon, 1978). The thyroid hormones are normally secreted into the lumen of the follicle where they are stored in colloid but in a state of hyperactivity they may be released directly into the blood (Kaplan, 1992). A small group of cells, the Parafollicular cells or c-cells are scattered throughout the gland. The Parafollicular cells secrete the calcium lowering hormone calcitonin (Nunez and Gershon, 1978). When the gland is inactive, the colloid is abundant, the follicles are large, and the cells lining them are flat. When the gland is active, the cells are cuboids or columnar (Ganong, 1995).
The principal hormones secreted by the thyroid gland are T₄ and T₃. Most of T₃ in the circulation is formed in the peripheral tissue by deiodination of T₄ catalyzed by 5’-deiodinases. Small amounts of reverse triiodothyronin (rT₃) are also produced by the action of 5’-deiodinases enzyme. Monoiodotyrosine and other compounds are also found in thyroid venous blood. T₃ is more active than T₄, whereas rT₃ is inactive (Pitt Rivers, 1955; Braverman et al., 1969; David et al., 1983; Takachev and Romenskaya, 1991; Gregory, 1997). The thyroid gland possesses a unique water-soluble glycoprotein named thyroglobulin. Thyroglobulin is synthesized in the thyroid cells and secreted into the colloid by exocytosis, the levels are higher in women compared with men, and they increase further in pregnancy (David et al., 1983; Gregory, 1997). Thyroglobulin serves as storage form of easily accessible thyroid hormones. This storage allows the thyroid gland to continue to secrete thyroid hormones, despite transient deficiencies in environmental iodine (Glinoer et al., 1990; Gregory, 1997). Thus the hormones remain bound to the thyroglobulin by peptide bonds until secreted. When they are hydrolyzed free T₄ and T₃ are
discharged into the capillaries (Ganong, 1995; Gregory, 1997).

1.2 Action of thyroid hormones

Thyroid hormones have played a role in vertebrate life since the days when primitive crossopterygian fish ruled the seas, and they have been found in all forms of extant vertebrates from the lamprey larva to modern man (Gorbman A., 1958).

Thyroid hormones influence and speed up many metabolic processes in the body. The rate of utilization of carbohydrates and lipids for energy is greatly accelerated. Although the rate of protein synthesis is increased, at the same time the rate of protein catabolism is also increased. They are essential for normal growth, mental development and sexual maturation. They also increase the sensitivity of the cardiovascular and central nervous system to catecholamines and so influence cardiac output and heart rate (Stanbury and Hetzel, 1980; Dillmann, 1990; Heyerdahl et al., 1991).

1.3 Thyroid hormone metabolism

1.3.a Thyroid hormone synthesis
Iodine is a raw material essential for thyroid hormone synthesis. The minimum daily iodine intake that is necessary to maintain normal thyroid function is: age 0-7 years 90 µg/day; age 7-12 years 120 µg/day; older than 12 years 150 µg/day; and pregnant and lactating women 200 µg/day (Wayne et al., 1964; Holman and McCartney 1991; WHO 1994). Iodine in the diet is absorbed rapidly by the stomach and the upper small intestine; the excess iodine is rapidly excreted by the kidney. The level of excretion correlates well with the level of intake, so it can be used to assess the level of iodine intake (Harrison et al., 1965; Koutras et al., 1980; Mao et al., 1990; Azizi et al., 1999). The biosynthesis and secretion of the thyroid hormones are as follows:

1- Iodine in the form of iodide ion is actively taken up by the thyroid gland from the blood circulation to the colloid (iodide trapping mechanism) approximately 25 fold of that in the plasma (Wolff, 1972). The salivary gland, gastric mucosa, ciliary body of the eye and mammary glands are also capable of concentrating iodide (Ganong, 1995). Uptake of iodide is blocked by a number of monovalent anions that compete with iodide for active transport into the thyroid, including chlorate, perchlorate, periodate, bi-iodate, nitrate and thiocyanate (Stanbury and Hedge, 1950; Funderburk and Middlesworth, 1967; Bourdoux et al., 1978; Day TK et al., 1972; Osman et al., 1983; Gaitan et al., 1983). The trapped iodide is oxidatively converted to iodine (Ganong, 1995; Gregory, 1997).
2- Tyrosine residues in the thyroglobulin are iodinated to form mono and diiodotyrosine (MIT and DIT) the two processes of oxidation and iodinated tyrosine are catalyzed by the enzyme thyroid peroxidase (TPO), with hydrogen peroxide (H₂O₂) as electron acceptor (Taurg et al., 1970; Pommier et al., 1974).

3- Two molecules of DIT are coupled to form thyroxine (T₄) and a molecule of DIT together with a molecule of MIT are coupled to give triiodothyronine (T₃) by an oxidative process in which also the enzyme thyroid peroxidase (TPO) is involved (Chopra 1978).

Ganong (1995) reported that, in normal human thyroid, much more T₄ than T₃ is synthesized and only traces of (rT₃) and other components are present. The synthesized hormones T₄ and T₃ still incorporated in the thyroglobulin are stored in the colloid of the thyroid follicle. Before secretion of the thyroid hormones, the follicular cells take up thyroglobulin by the process of pinocytosis (Chopra, 1978). The peptide bonds between the iodinated residues and the thyroglobulin molecule are broken by proteases in lysosomes, and then T₄, T₃, DIT and MIT are liberated into the cytoplasm (Wollman, 1969). The free T₄ and T₃ then cross the cell membrane and are discharged into the capillaries. MIT and DIT are not secreted into the blood, but they are deiodonated by the enzyme iodotyrosine deiodonase. The gland reuses the products of this reaction, iodine and tyrosine (Wollman, 1969; Chopra, 1978).
Some drugs reduce the conversion of $T_4$ to $T_3$ like: glucocorticoids, iodine, beta-blocker and amiodarone (Edwin and Alan, 2002).

### 1.3.b Thyroid hormone degradation

The normal secretion from the thyroid gland contains approximately 80% $T_4$ and 20% $T_3$. The biologically active form of thyroid hormones is $T_3$ and is derived from $T_4$. The various metabolic pathways of thyroid hormone are adapted to regulate $T_4$ to $T_3$ conversion at the target tissue level as well as to preserve $T_3$ in critical tissues, such as the brain, in times of reduced thyroid hormone production (Larsen, 1982; Brent, 1994; Xue Yic et al., 1994). Hepatic sulfation or glucuronide formation of thyroid hormone metabolites allows their excretion by the kidney or in the bile. These pathways allow for retention of iodine which is especially important in areas of iodine insufficiency (Gregory, 1997). The deiodinase enzymes have distinctive characteristics based on tissue distribution. The full activity of the thyroid hormones required deiodination of $T_4$ to $T_3$. $T_3$ is produced by the thyroid gland but results mainly from the peripheral deiodination of $T_4$ catalyzed by iodothyronine 5-deiodinaze enzyme (Kohrle et al., 1991; Berry et al., 1991).
1.4 Thyroid disorders

An individual with an appropriate amount of thyroid hormones is said to be euthyroid (eu = well, suitably). The most common cause of thyroid disorders worldwide is iodine deficiency leading to goitre formation and hypothyroidism. In areas not deficient in iodine, autoimmune processes are believed to be the basis for most cases of thyroid disease ranging from hyperthyroidism to hypothyroidism (Tunbridge, 1986).

Goitre refers to any enlargement of the thyroid gland, with or without disturbance of the function. The deficiency of thyroid hormones production T4 and T3 known as hypothyroidism. The symptoms of which include fatigue, hair loss, dry skin, weight gain despite poor appetite, cold intolerance, deep voice (horseness), bradycardia and myxoedema (Evered et al., 1973; Ermans et al., 1980; Wilansky and Gresiman, 1989; Martin, 1997).

Abnormal high plasma concentration of T4 and T3 suppress TSH secretion producing the syndrome hyperthyroidism. The clinical features of which are tremor,
weight loss, tiredness, excessive sweating, diarrhea, nervousness, heat intolerance and tachycardia (Martin, 1997; Thomas and Jerome, 1997).

An immunogenetic background of Grave’s disease and Hashimoto’s thyroiditis are part of the spectrum of autoimmune thyroid disease. Grave’s disease is a common cause of hyperthyroidism and is an autoimmune disease. Hashimoto’s thyroiditis, an autoimmune disease, is the most common cause of hypothyroidism, caused by defective peroxidase activity resulting in decreased thyroid hormone synthesis and increased TSH secretion, and ultimately hypothyroidism (Matsuura et al., 198; Pop et al., 1995; Brown et al., 1996).

Some drugs may cause hyperthyroidism or hypothyroidism like interferon and interleukin (table 1.1) (Edwin and Alan, 2002).

1.5 Goitre (endemic goitre)

Goitre is an enlargement of the thyroid gland and can be viewed as an adaptation of man to iodine deficiency (Studer and Greer, 1965). A normal thyroid gland should have the minimal size compatible with euthyroidism under
conditions of normal iodine intake (100-150 µg/day). The gland would be non-palpable or barely palpable. For practical purposes, the definition of goitre of Perez et al., is recommended: “A thyroid gland whose lateral lobes have a volume greater than terminal phalanges of the thumbs of the person examined will be considered goitrous (Perez et al., 1960).

Harrison et al., (1965), Thilly et al., (1980), and John and Gaitan (1990); reported that a diet containing inadequate amount of iodine hinders the synthesis of thyroid hormones. When the iodine intake is inadequate; reduction in the urinary iodine output will be the first sign reflecting this condition. If the reduction of iodine intake continues or worsens, a fall in serum T<sub>4</sub> and a rise in TSH will be the result; these changes tend to stimulate better utilization of the

Table 1.1 Drugs Affecting Thyroid Function (Edwin & Alan, 2002)

<table>
<thead>
<tr>
<th>Effect</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>May cause hypothyroidism</td>
<td>Lithium, iodine (all forms, including kelp, contrast media, etc), interleukin-2, interferon-</td>
</tr>
<tr>
<td>Effect</td>
<td>Examples</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>May cause hyperthyroidism</td>
<td>Iodine, interleukins, interferons</td>
</tr>
<tr>
<td>Reduce conversion of T4 to T3</td>
<td>Glucocorticoids, amiodarone, iodine, propylthiouracil, beta-blockers.</td>
</tr>
<tr>
<td>Suppress thyroid stimulating hormone</td>
<td>Dopamine, phenytoin, dobutamine, glucocorticoids, bromocriptine, octreotide.</td>
</tr>
<tr>
<td>Increase clearance of T4</td>
<td>Carbamazepine, phenytoin, rifampin, phenobarbitol</td>
</tr>
<tr>
<td>Reduce binding of T4 to thyroid-binding globulin</td>
<td>Salsalate, salicylates, nonsteroidal anti-inflammatory drugs, furosemide, heparin</td>
</tr>
<tr>
<td>Cause increased thyroid-binding globulin</td>
<td>Estrogens, tamoxifen, methadone, heroin, 5-fluorouracil, clofibrate, perphenazine, mitotane</td>
</tr>
<tr>
<td>Reduce thyroid-binding globulin</td>
<td>Androgens, glucocorticoids, aspariginase.</td>
</tr>
<tr>
<td>Influence absorption of thyroxine</td>
<td>Cholestyramine, aluminum hydroxide, ferrous sulfate, sucralfate, cation exchange resins</td>
</tr>
</tbody>
</table>

Available iodine. A prolonged TSH stimulatory effect will be followed by thyroid enlargement (goitre).

The identification of thyroid size by gross clinical examination (palpation) has been the most widely used test
particularly. The method recommended by the World Health Organization (Perez et al., 1960; Thilly et al., 1980). In the WHO method classification of goitre was based on staging of the size of the thyroid gland into:

- Stage 0: not palpable (no goitre)
- Stage I: Palpable; visible only with the head raised
- Stage II: easily visible with the head in normal position
- Stage III: Visible at a distance (very large goitre)

The total goitre rate is the prevalence of stage I-III. The visible goitre rate is the prevalence of stage II-III. An endemic goitre has been defined as greater than 10% prevalence of goitre in a defined geographical region (Perez et al., 1960; Delange, 1974; John and Frints, 1990). Recently it has been published by International Council for Control of Iodine Deficiency Disorders (ICCIDD) (1999); that a total goitre rate of 5% or more in school age children indicates a public health problem. The most well-known and most serious areas of endemic goitre are located in mountainous region: the Andes, the Himalayas, and the Alps. The disease is also observed in regions of low altitude such as Finland and in Coastal areas such as in Japan, Greece. Also it has revealed the existence in Africa, Asia and South America of very large endemic goitre (Stanbury and Hetzel, 1980).
Thyroid dysfunctions:

- **High TSH**
  - Low T4: Primary hypothyroidism (rarely seen in secondary hypothyroidism)
  - Normal T4: Subclinical hypothyroidism
  - High T4: TSH-mediated hyperthyroidism
    - Low T4: Euthyroid hypothyroxinemia
      - No further testing (?) Repeat labs
    - Possible secondary hypothyroidism
      - Medications/bindin... inhibitors
- **Normal TSH**
  - Normal T4: No further testing (?) Repeat labs
    - High T4: Euthyroid hyperthyroidinemia
- **Low TSH**
  - Low T4: Central hypothyroidism
    - Euthyroid sick syndrom
  - Normal T4: Subclinical hypothyroidism
    - Elderly patients may have increased risk of atrial fibrillation
  - Low RAIU**
  - High T4: Thyrotoxicosis
    - High RAIU**
      - Toxic diffuse goiter (Graves' disease). Toxic multinodular goiter. Toxic adenoma. Functioning follicular thyroid carcinoma. Lithium induced hyperthyroidism. Motar pregnancy hyperemesis gravidarum choriocarcinoma

---

* TSH <0.03mU/L generally indicate thyrotoxicosis or tendency to thyrotoxicosis
** Radioactive Iodine Uptake in 1^2^3^I thyroid scan
*** Production of bio-inactive TSH measured in some RIA could result in mild TSH elevation
Figure 1.1 Algorithm for interpreting thyroid function tests (Edwin & Alan 2002)
Ermans (1986) reported that goitre is critically influenced by age and sex. In severe endemias the disease appears very early. Its prevalence increases considerably after the age of 3 and attained a peak value during puberty (Delange, 1974). From the age of 10 years the prevalence is higher in girls than in boys; the difference between the sexes is even more marked in adults. In both sexes goitre prevalence decreases during adulthood, but the decline is sharper in men than in women.

Bellis et al. (2000) added: In addition to iodine deficiency, other factors linked to sex, age, and lifestyle may contribute to endemic goitre. Also ethnicity is a significant factor in goitre development. Also congenital dyshormonogenesis is likely to be another factor in the development of goitre (Mukhtar, 1974).

1.6 Goitrogens

Many observations indicate that iodine deficiency may be present in certain populations but with absence of any abnormal prevalence of goitre (Delange, 1974; Choufoer et al., 1965). However, in some adjacent areas with a similar intake, severe endemic goitre occurs. These data strongly suggest that some goitrogenic factors in the diet or
environment, other than iodine deficiency could play a critical role in the pathogenesis of the disease (Delange et al., 1968; Ermans et al., 1972), McLaren and Donald (1979); defined goitrogens as substances which increase the thyroid gland size by interfering with the normal production of the thyroid hormones.

Natural goitrogens were first found in vegetables. Vegetables of genus Brassica possess goitrogenic properties in animals. Their antithyroid action is related to the presence of thioglucosides, which after digestion release thiocyanate and isothiocyanate (Ermans et al., 1980; Greer, 1960).

An important group of natural goitrogens is the cyanoglucoside, which have been found in several staples (Cassava, Maize, bamboo shoots, sweat potatoes, Lima, beans). (Langer, 1960). After ingestion these glucosides release cyanide, which is detoxified by conversion to thiocyanate.

Elmahdi and his co-workers, (1983); reported some vegetables found to be goitrogenic in laboratory animals, cabbage, turnip, radish, peanut, cassava, onion and peas. Other independent researchers considered millet to be a cause
of goitre in the Darfur area of Sudan where iodine deficiency is known to be prevailing (Osman et al., 1983)

Ekpechi et al., (1966); considered cassava one of the basic food stuffs in tropical areas has a definite goitrogenic activity. Raghunath and Bala (1998) in England studied populations living in goitre endemic areas consuming foods rich in a variety of goitrogens of different potencies. They found a significant correlation between the goitrogen cyanide and the sever hypothyroidism in the subjects studied.

A large number of goitrogenic factors may be present in polluted drinking water. High minerals content, particularly of magnesium and calcium salts, and bacterial contamination have been incriminated. An antithyroid substance has been extracted from cell-free filtrates of E. coli cultures. (Vought et al., 1974). Bacteriological studies from goitrous villages in Greece revealed that the drinking water was significantly more often polluted with Escherichia coli than the water from the non-goitrous localities (Malamos et al., 1971). A similar relationship had been previously demonstrated by Vought et al., (1967) in Richmond country in Virginia USA, where goitre exists despite adequate iodine supplementation. They also showed anti-thyroid activity in
cultures of *E. coli* from a polluted stream in that area of high endemicity.

Day and Powell (1972) correlated the prevalence of endemic goitre in 17 Himalayan villages with concentration of iodine, fluoride, calcium, magnesium and the total hardness of the drinking water. They found uniformly low iodine, but a positive correlation between goitre prevalence and fluoride, calcium, magnesium and total hardness.

Elmahdi *et al.*, (1983) reported that the endemic goitre in the Sudan is due mainly to iodine deficiency, but the role of goitrogenic factors in food and water cannot be completely excluded.
1.7 Iodine deficiency disorder (IDD)

Human require iodine, which is an essential component of the thyroid hormones $T_3$ and $T_4$. According to the Food and Nutrition Board of the National Research Council (1970); the optimum requirement for adult is in the range of 150-300 µg/day. A safe supply is estimated to be 50-1000 µg/day. Failure to have adequate iodine leads to insufficient production of these hormones which affect many different parts of the body, particularly heart, liver, kidney and developing brain (Stanbury and Hetzel, 1980; Hetzel, 1989; Dillman, 1990). Inadequate hormone syntheses adversely affect these tissues resulting in the disease state known collectively as the iodine deficiency disorders (IDD). Globally 2.2 billion people (38% of the world’s population) worldwide live in areas with ID. WHO in 1993 reported that IDD affect some 320 million people mainly in developing countries. These consequences include individually: goitre (enlarged thyroid), hypothyroidism, loss of energy. In children hypothyroidism causes impaired mental and physical development, mental retardation, physical deformities and growth retardation (cretinism). Cretinism characterized by retardation in physical and mental development (fig.1.2) Endemic cretinism is geographically associated with endemic goitre and iodine deficiency. It includes neurological cretinism and hypothyroid cretinism. Neurological cretinism characterized by mental deficiency, deaf-mutism and
abnormalities of gait. Hypothyroid or Myxedematous cretinism is typified neurologically by retarded psychomotor development and
slow psychomotor activity, but not deaf-mutism (fig. 1.3). They have severe stunting of growth, coarse facial features and myxedema and commonly have musculoskeletal disorders including scoliosis and hypotrophic muscle. The typical myxedematous cretin has a less severe degree of mental retardation than the neurological cretin. It has all the features of extremely severe hypothyroidism present since early life, as in non recognized sporadic congenital hypothyroidism: severe growth retardation, incomplete maturation of the features including the naso-orbital configuration, atrophy of the mandibles, puffy features, myxedematous, thickened and dry skin, dry
and rare hair, eyelashes and eyebrows and much delayed sexual maturation. (Pharoah et al., 1971). Soriguer et al., (2000) conducted audiometry in 150 children and related the results to thyroid volume, thyroid hormones and urinary iodine. The results suggest that iodine deficiency can cause not only goitre but can impair the auditory threshold in school-age children.

**In pre-pubertal years** hypothyroidism leads to short stature and may lead to delay in sexual maturity. However an interesting syndrome described by Van Wyk and Grumbach (1960) occurs: Precocious menstruation and galactorrhea in girls with juvenile hypothyroidism. **In adult women,** hypothyroidism results in changes in cycle length and amount of bleeding. Menorrhagia is a frequent complaint. There may be episodes of amenorrhea interspersed with periods of heavy vaginal bleeding, and in severe hypothyroidism anovulation is frequent. Ovulation and conception can occur in mild hypothyroidism.

**In pregnant Women** in iodine deficient areas face increased demands for iodine both during pregnancy and lactation, causing exaggerated iodine loss over years and consequent goiter. Frequently, the goiter continues after pregnancies cease, and in later years may become multinodular and cause hyperthyroidism. The iodine deficiency may also make the mother hypothyroid. Pregnancy can occur in women who are hypothyroid, but they will have greater difficulty in carrying a normal fetus to term. Pregnancy is associated with abortions in the first trimester, stillbirths, prematurity or mentally retards children. On society it lowers productivity and higher demand on social services (Barakat and Ingbar, 1965; DeGroat and Stanbury, 1975; Mc Minn, 1984; Hetzel, 1993).

**The cardiovascular** features of severe hypothyroidism are including: cardiomegaly, Bradycardia and low-voltage complexes on the electrocardiogram (ECG).
1.3 Myxedematous endemic cretinism: Four inhabitants aged 15-20 years: a normal male and three females with severe hypothyroidism with dwarfism, retarded sexual development, puffy features, dry skin and hair and severe mental retardation.
Figure 1.4 a dwarfed cretin woman with a "barefoot doctor" of the same age (35 years).
Figure 1.5: Three women with typical endemic goitre
Figure 1.6: A mother and child: the mother has a large goitre and the effect is cretinism in the child
1.8 Iodine deficiency in Sudan

Endemic goitre in the Sudan was first reported in 1952 by Woodman, who described a small area inhabited by the Azande in South West Sudan near the Zaire border. He also described other neighboring areas with a high goitre rate in the South of Malkal, among the Neur Tribe, around El Damer in the Northern Province and in Darfur (Woodman, 1952).

Kambal (1969); completed an extensive survey in 1967 comprising 17470 people in Darfur province and found that 57.7% were goitrous and that 18.5% of these had large goitre. In Khartoum, 12.6% of 5566 subjects had goitre, large goiter was in 0.6%. Based on the early comprehensive investigations that suggesting the aetiology of endemic goitre in the Sudan Greig and his co-workers, (1970) concluded that the major cause of endemic goitre in the Sudan was iodine deficiency. Osman and Fatah (1981); conducted a study in Darfur. They suggested that the high endemicity of goitre in this province may be due not only to iodine deficiency but also to other factors such as protein energy malnutrition, low vitamin A intake, high sodium, potassium and iron contents of drinking water and high consumption of millet (*Pennisetum typhoides*), which is the staple diet in that area. Before that Mukhtar (1974), reported that congenital dyshormonogenesis is likely to be an important contributory factor in the development of some cases of goitre in the Sudan.

Eltom (1984); showed that, the prevalence of goitre among school children in Darfur was 86%, in the central state (Kosti) 75% and in Khartoum 18%.

In other study, by Moreno *et al.*, (1993) conducted in Darfur among 20 neonates and 190 children aged 1 month to 7 years, the mean serum concentration of thyroxin (T₄) was found to be very low and serum TSH was high, and the incidence of hypothyroidism was estimated at 25%. They concluded that, iodine deficiency and goitrogenic action of millet were responsible for the higher frequency of hypothyroidism in children older than 2 years of age.
New study conducted by Abdel Gafar (2005), in Kosti, Rabak and Jabal Awlia on 300 schoolchildren aged between 6-18 years showed that the prevalence of goiter was 54.7%. It was 54% in Kosti, 65% in Rabak and 45% in Jabal Awlia.

Study on the effect of loss in sweat on the iodine deficiency by Mao et al., (2002) concluded that profuse sweating can result in iodine deficiency. By this study he confirmed other study conducted in 2001. The authors analyzed 208 sweat samples and measured urinary iodine from 13 male high school soccer-team players and 100 sedentary peers in Taiwan over eight days. He found that a one-hour game resulted in the loss of 52 µg of iodine. The ratio of sweat loss to urinary daily loss of iodine was 0.75. These studies are important in the high temperature climate in Sudan.

1.9 Strategies for the prevention of IDD

The solution of IDD is relatively simple. A teaspoon of iodine is a requirement of a person in a lifetime, but because iodine cannot be stored for long periods by the body, tiny amounts are needed regularly. The methods available for iodine supplementation or prevention of IDD fall into two categories: (1) Measures for the whole population-iodized salts, bread and water, (2) perspective measures suitable for children and women at reproductive age are the iodized oil and iodide tablets (Hetzel, 1989).

**Iodized salt:** There are two form of iodine, which can be used to iodized salt: iodide as an iodide salt, and iodate as an iodated salt. Iodate is less soluble and more stable than iodide and is therefore preferred for tropical moist conditions (Hetzel, 1989). Iodization of salt is the preferred approach for supplementation in iodine deficient population. It is used by all section of community irrespective of social and economic status. Salt iodization was first used in Switzerland in 1922 (Mabyou et al., 1984; ICCIDD 1990; WHO, 1994). Iodized salt should be consumed within six months of purchase.

**Oral iodized oil** is effective and acceptable for treating iodine deficiency in adult (Tonglt et al., 1992; Elnagar et al., 1995). Iodized oil was first used by McCullough (1963); in regions in New
Guinea where salt iodization was impractical. The effect of such treatment was demonstrated further by Hennessy (1964); and Buttfield et al., (1965); they showed a significant reduction in goitre size and effective correction of iodine deficiency which lasted four-and-half year.

The major groups requiring iodized oil are: women of reproductive age, children up to 5 years of age and children up to completion of adolescence (16 years). Iodized oil should be avoided over the age of 45 because of the possibility of precipitating hyperthyroidism (Hetzel, 1989).

Oral administration of single doses of iodized oil capsules is a good alternative for injectable form. Its administration requires less technical training, fewer instruments and less time. Also certain hazards are avoided. It used once a year, by a responsible person who would not need to be technically trained (Elnagar et al., 1995).

Iodized bread has been used in Holland and in Australia (Clement et al., 1970).

Iodized water may be more convenient than iodized salt and there is additional benefit of antiseptic action. This method is appropriate at village level if a specific source of drinking water can be identified, otherwise there is a heavy cost, as less than 1% of a general water supply is used for drinking purposes. Two drops of concentrated iodine solution are added to 10 liters of drinking water daily (Hetzel, 1989).

Iodized eggs: Recent experiments have also introduced iodization of chicken eggs, to provide 150-250 µg iodine per egg. Eggs are placed in an iodine-containing bath and iodized by iontophoresis. The cost of this fortification is minimal.

Iodized fish sauce: Direct addition of iodine to fish sauce at the household level has been attempted, but has not been popular. Iodine can also be added in the manufacturing process. In a pilot project in Thailand the producer buys fish sauce concentrate, mixes it with salt water, adds a concentrated solution of potassium iodate to the large mixing bath, and then bottles the product. This approach works better than direct addition to individual bottles, which
occasionally resulted in precipitation. The iodine concentration of the iodized fish sauce was apparently in the desired range (IDD NEWS, 2000).

**Iodized noodles and bananas** instant noodles and one brand dried bananas have been fortified with iodine, vitamin A, and iron by adding these as a premix. By dipping the bananas in a solution that provides potassium iodide (30-100 µg iodide), vitamin A (200 µg), and iron (2 mg), before final heating and packaging. This method is being successfully applied in a demonstration factory. The cost with iodization is about 30% higher, mainly because of packaging. The system is flexible in that the amounts of micronutrients can be easily changed.

The iodization process is a coating and probably not a chemical reaction.

The introduction of other vehicles for iodization is innovative and interesting. They may have application in specific local circumstances and in relation to particular cultural habits. A general concern about vehicles other than essentials, such as salt and water, is that their use may be uneven within the population, favoring the more affluent male adults rather than the rural poor women and children, the primary targets for preventing iodine deficiency.

Generally Hetzel, (1989) suggest that the iodized salt is appropriate measure in mild IDD goitre endemias (iodine excretion is more than 50 µg/g of creatinine), to maintain the thyroid hormones level adequate for normal mental and physical development. In case of moderate IDD: Goitre endemias with an average urinary iodine excretion of between 25-50 µg/g of creatinine. In these circumstances adequate thyroid hormone formation may be impaired. This group is at risk of hypothyroidism, but not of overt cretinism. Iodized salt may be adequate, but if effective salt iodization cannot be achieved quickly, iodized oil is indicated. However, in sever IDD: Goitre endemias with an average urinary iodine excretion below 25 µg/g of creatinine. Endemin cretinism is a serious risk in such a population. Iodized oil is required for quantitative correction and will need to be continued if subsistence agriculture continues in the area.

1.10 Iodine
Iodine was discovered by Curtois in 1812 on observing violet fumes rising when saltpeter pots were heated. It was named “Iode” in French after the Greek word “loeides” meaning violet-colored. It exists as shining flakes that can be easily crushed. The boiling point 184.4° C, and it is only sparingly soluble in water: 0.16 grams dissolves in 1 kg water at 0°C and 4.4 grams at 100°C. It dissolves in many organic solvents giving a brown to violet color (Lauterbach et al., 2000).

1.10.1 Iodine distribution

The ocean is the primary source of iodine in the world. The concentration of iodine in the sea water is about 50-60 µg/litre, about the same as in human serum. The average iodine concentration in the earth is 300 µg/kg and in the air is about 0.7 µg/m³ (Fleischer et al., 1974). The atmospheric iodine constitutes an important part of the iodine cycle (Vought and Brown, 1970). About 14-20 µg of iodine can be added to daily iodine intake, since “standard man” breathes 20 m³ of air per day (Koutras et al., 1980). Rain contain much more iodine (1.8 – 8.5 µg iodine/liter) than does the air (Duce et al., 1963).

Iodine is widely but thinly distributed in rocks, soil, water, plants, animal tissues and foodstuffs. It almost never occurs in the free form, but in combined with other elements, usually as inorganic salts. The few sites where it is concentrated include seaweeds, occasional underground waters, from deep oil well drilling, and some minerals springs. The largest concentration is in the natural deposit of sodium nitrate “cliché” in Northern Chile. The iodine in natural source is underground brine associated with oil and gas deposits in Japan, where iodine occurs most frequently as sodium iodide (Na I) at 50-150 ppm.

In land regions far from the ocean have the greatest risk of iodine deficiency. Mountainous areas have the most serious iodine deficiency such as in Alps, Andes, Himalayas and Jabal Marra, where iodine in the soil has been washed by rain and glaciers. However, iodine deficiency is observed in regions of low altitude such as Central Africa, Central Asia and part of Central Europe. Iodine deficiency is also associated with areas exposed to frequent flooding and
in large river deltas such as those of the Ganges, Yellow River White Nile River and Rhine
(Eltom, 1984; Dunn and Haar, 1990).

1.10.2 Iodine content of food

Seafood is usually a good source because the sea contains considerable amount of iodine. Other foods vary tremendously in iodine content, depending on their source and what may have been added. Plants grown in iodine-deficient soil do not have much iodine, nor does meat or other products from animals fed on iodine-deficient plants (Koutras et al., 1980). Because the breast concentrates iodine, dairy products are usually a good source, but only if the cow get enough iodine. Higher values of iodine in milk during winter, and lower during summer, have been reported (Broadhead et al., 1965). Source of iodine in the diet are sea foods, roe, eggs, papayas, mangoes, pin apple, onions, eggplant, potatoes, oats, leaf lettuce, beans and any thing grown near the ocean or sea (Michell, 1999). Herbal sources are kelp, which is favorite source of iodine supplementation. The main natural sources of dietary iodide are seafood. (200-1000 µg/kg) and seaweed (0.1-0.2% µg/liter) (Hetzel and Maberly, 1986).

Iodine is added to the food and it is also lost by cooking. It has been observed that, the iodine content of fish was reduced 20% by frying, 23% by grilling and 58% by boiling (Harrison et al., 1965).

1.10.3 Chemical forms of iodine

Salts such as potassium iodide (KI) and potassium iodate (KIO₃) are the most important commercial source of iodine. The most common is KI, which is soluble in water, ethanol and several other organic solvents. KIO₃ with KI is the most common form used to iodized salt.

The common organic iodine derivatives are methyl iodide (CH₃I), diiodomethane (CH₂I₂), iodoform (CHI₃) and ethyl iodide (C₂H₅I). Some aromatic compounds of commercial interest are: thymol iodide (C₂₀H₂₄I₂O₅), Iodobenzene (C₆H₅I) and 4-iodophenol (C₆H₅IO).

1.10.4 Iodine usage
Iodine used for various purposes such as x-ray contrast media, biocides and iodophors e.g. povidone iodine which used as a skin cleanser. Iodophors are also used in cosmetics, adhesives, paints, wood preservation, inks and starches to protect against particular organisms.

Iodine used for water purification as 1ppm sterilizes water. Iodine has wide use in photography. Iodine is a major component of certain dyes particularly erythrosine (tetraiodofluoroscein). The manufacture of pharmaceuticals, agrochemicals and dyestuffs makes extensive use of iodine derivatives.

1.10.5 Importance of iodine for human

Iodine is an essential micronutrient for human survival. It is needed for growth and development, even before birth. The importance of iodine in human nutrition is due to the fact that it is an essential component of the thyroid hormones, thyroxine and triiodothyronine, which are needed for normal development and functioning of the brain and nervous system, and for maintenance of body heat and energy. Thyroxine stimulates cell oxidation and regulates basal metabolic rate, apparently by increasing oxygen uptake and reaction rates of enzymes handling glucose, thus iodine indirectly exerts a tremendous influence on the body’s over all total metabolism (Williams, 1986). Very small amounts of iodine (100-300 µg/day) are sufficient to satisfy daily needs and enable the body to work properly (Bourdoux et al., 1985).

1.10.6 Effect of excess iodide

Iodine participates not only as a requisite substrate for thyroid hormone biosynthesis, but also in many pharmacological actions within the gland, and the effect of iodide on the thyroid is a combination of the effect of the pharmacological action of iodide and the effects of iodide as substrate for thyroid hormone. The effect of excess quantities of iodide on hormone synthesis varies depending upon a number of factors- the iodide dose, the duration of exposure to iodide, species variation and the functional state of the gland. Excess doses of iodide defined as being
the amounts that are greater than necessary for the formation of normal quantities of thyroid hormones.

Moderate dose of iodide leads to decrease in the percentage uptake of administered iodide; however it also results in an increase in the absolute rate of organic iodination and thyroid hormone synthesis. A large dose of iodide decreases both the percentage incorporation of administered iodide and the absolute rate of organic iodine formation (The Wolff-Chaikoff effect). A very large dose of iodide saturates the mechanism for active transport of iodide. The inhibitory action of excess transport of iodide (The Wolff-Chaikoff effect) is temporary. The inhibition of organic iodine formation disappears spontaneously despite a continued administration of the iodide and the formation of organic iodine increase. This adaptation seems to occur because, with continued iodine administration, iodide-transport activity decreases and intrathyroidal iodide concentration becomes insufficient to continue a complete Wolff-Chaikoff effect (Shigenobu and Sidney, 1986).

Acute increase in iodine ingestion in humans has been shown to result in slight, but significant, transient decrease in the serum concentrations of both T₃ and T₄. After this acute decrease the serum hormone levels return to normal. In some particularly susceptible individuals continued exposure to excess iodine induces sustained inhibition of hormone synthesis leading to goitre and myxedema (Maturlo, 1980).

1.10.7 Iodine measurement

The dietary iodine intake can be measured by direct or indirect methods:

1.10.7a Direct measurement of iodine intake

Daily iodine intake can be measured by collecting a duplicate of the foods ingested by the patient during the period of the study (Koutras et al., 1970). The methodology adapted for
the measurement of iodine in food is driven from the measurement of iodine in blood, which is based on the catalytic effect of iodide on the coupled reduction of the ceric ion by arsenous acid.

1.10.7b Indirect measurement of iodine intake

Urinary iodine

With regard to the compartment analysis of iodine metabolism, the inorganic iodine is either accumulated in the thyroid gland or excreted in the urine (Degroot, 1966). Since the renal iodine clearance rate is constant, urinary excretion of iodine fluctuates according to the plasma concentration of iodide, which in turn, depends on the amount of iodide absorbed from the gut. This fact is well illustrated by the inverse relationship between the thyroid uptake and the urinary excretion of radio iodine in various thyroid conditions (Beckers & Delange, 1980). Since the faecal excretion of iodine is relatively constant, the 24-hours urinary iodine excretion satisfactorily reflects the dietary iodine intake.

It has been found that in the same subject, the excretion of iodine varies considerably from day to day according to the variation of the iodine intake. Negative balance may be persisting for several weeks (Vought et al., 1963).

In practice collection of 24-hours urine sample is difficult and may give rise to misleading results since the investigator is not always sure about the accuracy of the urinary collection.

The excretion of iodine per gram of creatinine in a single specimen has been proposed and successfully used in different studies (Vought et al., 1963). It has been recommended by the WHO that, the iodine intake is to be estimated by measuring the concentration of iodine in the urine, as μg iodine per 100 ml urine, because it is simpler and has proven more reliable than relating it to creatinine (Bourdoux et al., 1985). Because subjects vary in the concentration of their urine, depending on the amount of liquid they have been drinking, the WHO recommended that, the concentration of urinary iodine in a given region should be measured by taking the
mean of at least 40 subjects (Dunn and Haar, 1990). Deficiency is defined as either severe (median UI < 20 µg/L), moderate (20-49 µg/L), or mild (50-99 µg/L); sufficiency is 100 µg/L or higher, and excess is > 300 µg/L. Table 1.2 shows the relationship between the iodine nutrition and urinary iodine excretion according to WHO, ICCIDD and UNICEF program (2001).

Table 1.2: The relationship between iodine nutrition and urinary iodine concentration

<table>
<thead>
<tr>
<th>Median Urinary Iodine Concentration (µg/L)</th>
<th>Corresponding Approximate Iodine Intake (µg/day)</th>
<th>Iodine Nutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>&lt;30</td>
<td>Severe deficiency</td>
</tr>
<tr>
<td>20-49</td>
<td>30-74</td>
<td>Moderate deficiency</td>
</tr>
<tr>
<td>50-99</td>
<td>75-149</td>
<td>Mild deficiency</td>
</tr>
<tr>
<td>100-199</td>
<td>150-299</td>
<td>Optimal</td>
</tr>
<tr>
<td>200-299</td>
<td>300-449</td>
<td>More than adequate</td>
</tr>
<tr>
<td>&gt;299</td>
<td>&gt;449</td>
<td>Possible excess</td>
</tr>
</tbody>
</table>

1.11 Aim of the study

The aims of the present study are:
1- To assess the prevalence of IDD in schoolchildren aged 6-18 years in Kosti, Rabak, Jabal Awlia and Elfetihab around the White Nile in Sudan by measuring urinary iodine excretion and serum thyroid hormones.
2- To estimate the iodine content in local water (Nile, Wells and Hafers)
3- To estimate the iodine content of the iodized salt available in the area of the study and to assess its shelf life.

Chapter Two
Materials and Methods
2 Materials and methods

2.1 Study area

This study has been conducted around the White Nile in Sudan. On the eastern bank of the Nile lie Rabak and Jabal Awlia. On the western bank of the Nile lie Kosti and Elfetihab.

This area is inhabited by a multitude of ethnically unrelated tribes. The staple food in rural areas is durra (*Sorghum vulgare*) and in urban areas are durra and wheat (*Triticum vulgare*), however common to all areas the diet contains a large amount of peanut oil, onion, peas and garlic vegetables. In accordance with some authors may contain goitrogenic activity (Elmahdi *et al.*, 1983). Fish is not usually available for all people due to economic factors.

The drinking water is either from the river or traditional wells. The White Nile River is dominated by a floating aquatic weed (*Water hyacinth*), form a perennial mat covering the river surface.

2.2 The study population

The study was carried out on a sample selected from governmental primary and secondary schoolchildren (both sexes) around White Nile during the period from February 2003 to march 2004.

Stratified random sampling technique was used to select the study samples. The area was divided into four zones (Kosti, Rabak, Jabal- Awlia and Elfetihab). From each zone two schools were randomly selected. One class from each school grade was chosen. A total sample of 293 schoolchildren from the selected eight schools constituted the subjects of the study. (Table 2.1)

<table>
<thead>
<tr>
<th>City</th>
<th>School</th>
<th>Gender</th>
<th>Age</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kosti</td>
<td>Primary</td>
<td>Male</td>
<td>12-16</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>primary</td>
<td>female</td>
<td>11-16</td>
<td>38</td>
</tr>
<tr>
<td>Location</td>
<td>Grade</td>
<td>Gender</td>
<td>Age Range</td>
<td>Number</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
<td>---------</td>
<td>-----------</td>
<td>--------</td>
</tr>
<tr>
<td>Rabak</td>
<td>Primary</td>
<td>Male</td>
<td>13-17</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Primary</td>
<td>Female</td>
<td>12-16</td>
<td>30</td>
</tr>
<tr>
<td>Jabal Awlia</td>
<td>Secondary</td>
<td>Male</td>
<td>13-18</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>Female</td>
<td>15-18</td>
<td>30</td>
</tr>
<tr>
<td>Elfetihab</td>
<td>Primary</td>
<td>Female</td>
<td>6-10</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>Primary</td>
<td>Male</td>
<td>6-10</td>
<td>52</td>
</tr>
</tbody>
</table>

Kosti, Rabak, Jabal Awlia, Elfetihab
Figure 2.1: Map of Sudan showing the White Nile, Blue Nile and the Nile River and the study area

2.3 Sampling of urine

Data were collected using special designed questionnaire, including information about name, zone, class, exact age, sex and type of drinking water.

Urine samples (about 25 ml) were collected in sterile plastic containers, refrigerated at -25°C till analysed. The samples were collected from Kosti, Rabak Jabal Awlia and Elfetihab.

2.4 The methods of measuring iodine in urine

Most available methods for urinary iodine determination include an initial step in which the urine is either digested in strong acid or ashed at high temperature. Following that step, iodide is measured by its catalytic action on the reduction of ceric ion (Ce⁴⁺) to the cerous ion (Ce³⁺) coupled to the oxidation of arsenite As³⁺ to As⁵⁺. This reaction called the Sandell-Kolthoff reaction (1937) has been diagrammed as follows:

\[ 2\text{Ce}^{4+} + 2\text{I}^- \rightarrow 2\text{Ce}^{3+} + \text{I}_2 \]
\[ \text{I}_2 + \text{As}^{3+} \rightarrow \text{As}^{5+} + 2\text{I}^- \]

The ceric ion has a yellow colour, while the cerous is colourless. Thus the course of the reaction can be followed by the disappearance of the yellow colour as the ceric ion is reduced. The reaction can conveniently detect iodide levels down to several nanograms. Because of its specificity and high sensitivity this reaction has been the basis for almost all chemical methods for the detection of iodine in the urine. Method E (karmarkar et al.,
1986) has been recommended by WHO and International Council for Control of Iodine Deficiency Disorders (ICCIDD) (John and Gaitan, 1993) use ashing for destruction of interfering substances which is more vigorous and avoids the explosion of perchlorate that used in other methods.

**Method E:**

**Equipments:** Oven, muffle furnace, water bath, colorimeter, centrifuge, timer.

**Solutions:**

1- Potassium carbonate: 17.5 grams of anhydrous potassium carbonate were dissolved in small amount of deionized water and diluted to 100 ml then stored in a polyethylene bottle.

2- Ceric ammonium sulfate, 0.005 N: ceric ammonium sulfate (3.17 grams) was dissolved in 500 ml of deionized water and 57 ml concentrated H₂SO₄, then diluted to 1000 ml.

3- Sodium meta-arsenite, 0.035 N: 2.27 grams of sodium meta-arsenite dissolved in 500 ml deionized water, and then added 46 ml concentrated H₂SO₄ and made to 1000 ml with deionized water.

4- Stock iodine solution: 168.5 mg KIO₃ dissolved in 100 ml of water, and then diluted with water to make a working standard of 5 µg/dl.

**Procedure:**

Urine sample was mixed to evenly suspend and sediment. 100 µl of each urine sample was pipetted into a 15 X 125 mm test tube. 100 µl of water were pipetted into a 15 X 125 mm test tube for a blank. Into a 15 X 125 mm tubes, 100 µl of each iodine standard were pipetted. A standard prepared as 2.5, 5, 10, 20 and 40 µg/dl To each tube 300 µl of K₂CO₃ were added, then the test tube placed in a rack and placed in the oven for drying at a temperature of approximately 80-100° C overnight. After the samples are dried in the tubes, the rack was removed and placed it into the muffle furnace for ashing at 600° C for two hours. The temperature let to come down and the rack removed from the furnace. When the tubes have cooled to room temperature, 3 ml of sodium meta-arsenite was added to each tube then the tubes were incubated for five minutes in a water bath at 56° C. after that 3 ml of ceric ammonium sulfate was added at 30 seconds intervals to each tube, mixed and replaced in the water bath. Twenty minutes after addition of the ceric
ammonium sulfate, transmittance at 420 m\(\mu\) was read in colorimeter against a water blank using stopwatch to keep a constant interval.

2.5 Sampling of water

From each location visited, eight water samples were collected into polyethylene bottles which had been washed in distilled water. The samples were as following:


2.6 The method for measuring iodine in water

The content of iodine in the collected water samples was determined by the same method as that for determination of urinary iodine. It also was determined by Khartoum State Water Corporation- Central laboratory to confirm the results.

2.7 Sampling of blood

The blood samples were collected from 41 students randomly (13 male and 28 female). From each 5 ml of venous blood were collected in an iodine-free vacutainers. The blood samples were collected by experienced doctor and nurse-staff to estimate the T\(_3\), T\(_4\) and TSH. Blood allowed clotting and the serum was separated and kept frozen at -20\(^\circ\)C.

2.8 The method for measuring the serum T\(_3\), T\(_4\), and TSH

T\(_3\) and T\(_4\) were measured by the standard method Radioimmunoassay (RIA) techniques for quantifying total levels of the thyroid hormones (Larsen, 1978). RIA is based on the reaction of a limited concentration of antibody with varying concentrations of antigen. The proportion of free and bound antigen, which arises as a consequence of using a limited concentration of the specific reagent (the antibody) is measured by using a radio-labeled antigen.

The specific binding site is provided by immunization of sheep with thyroxine-albumine and triiodothyronine-albumine conjugates synthesized for this purpose.
Analino Naphthalene sulfanilic acid (ANS) is added to prevent binding of the antigen (T$_3$ or T$_4$) to the endogenous binding proteins without significantly altering its interaction with the antibody.

Separation of bound fraction from unreacted fraction is enhanced by adding second antibody (donkey anti-sheep serum). Polyethylene glycol (PEG) is added to the complex to obtain fine separation.

**Thyroid Stimulating Hormone (TSH)** was measured by a sensitive Immunoradiometric assay (IRMA). This method based on the reaction of excess antibody with varying concentrations of antigen, this give rise to a corresponding increase in bound antibody.

IRMA technique using solid phase (monoclonal) first antibody and $^{125}$I labeled second antibody with two simple washing steps to minimize the non specific binding (blank).

A sheep anti-TSH antiserum and a mouse monoclonal anti-TSH antibody have been used as the basis for a specific and sensitive IRMA for human TSH.

The labeled antibody is prepared by radioiodination of a purified monoclonal antibody, using chloramine T and subsequently is purified on Sephacryl s-300. The minimum detectable concentration was 0.01 to 0.03 mU/l.

**2.9 Sampling of salt**

Salt samples were collected from the market. Twelve different samples with different manufacturing date had been collected from salt packaging in high density polyethylene (HDPE). Eight samples were recently manufactured analyzed immediately, then stored for 6 and 12 months at the same environment available in the houses then analyzed second and third time. The other four samples were manufactured before 6 months, analyzed immediately and after 6 months.

The samples had been crystallizing during storage. Five samples from the core of crystal had been analyzed also.

Six samples were collected from other type of iodized salt which was packaging in low density polyethylene (LDPE). These samples were recently manufactured and have been analyzed immediately and after 6, 12 and 18 months.

**2.10 The method for measuring iodine in salt**
Iodine is available as KI in the iodized salt. It was analysed by titration with potassium iodate. This method is the official method for the assay of potassium iodide (Beckett and Stenlake, 1975). Reaction between KIO\textsubscript{3} and excess KI in acid solution results in liberation of iodine which can be titrated with sodium thiosulphate solution.

**Method:** Accurately 1.3 g of AnalaR potassium iodate was weigh. Dissolved in water and adjust the volume to 250 ml in volumetric flask. 25 ml from the solution was pipetted into a conical flask, and then 2 g of the iodized salt was added and diluted sulphuric acid 4 ml. This solution was titrated with 0.1N sodium thiosulfate solution.

\[
\text{IO}_3^- + 5\text{I}^- + 6 \text{H}^+ \rightarrow 3\text{I}_2 + 3\text{H}_2\text{O}
\]

\[
3 [\text{I}_2 + 2\text{e} \rightarrow 2\text{I}^-]
\]

\[
3[2\text{S}_2\text{O}_3^{2-} \rightarrow \text{S}_4\text{O}_6^{2-} + 2\text{e}]
\]

\[
\text{KIO}_3 \equiv 3\text{I}_2 \equiv 6\text{e}
\]

214.0 g KIO\textsubscript{3} = 6000 ml N

3.567 g KIO\textsubscript{3} = 1000 ml 0.1N Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3}

**2.11 Statistical analysis**

One-way analysis of variance (ANOVA), Scheff's test and T-test were used for comparison of means. Chi-squared test for comparison of frequencies and proportions were performed. All statistical procedures were conducted with the Statistical Package for Social Sciences (SPSS, for windows release 7.5).
Chapter Three

The Results

The results

3.1 The results of urinary iodine excretion

Table 3.1 illustrates the levels of iodine excretion (UIE) in Kosti. The overall median urinary iodine excretion was 0.54 µg/dl. The UIE was higher in male than that in female with significant difference (p-value 0.013). The median UI in male and female was 0.63 µg/dl and 0.5 µg/dl respectively (fig.3.1). Fig 3.2 Shows that 63.6% of the male student
and 92.1% of the female in Kosti excreted UI less than 2 µg/dl. None of the female and 18.2% of the male excreted UI more than 10 µg/dl.

Table 3.3 and figure 3.3 show that the median urinary iodine excretion in Rabak was 5.66 µg/dl. It was 2.85 µg/dl in male and 11.03 µg/dl in female which illustrated significant difference between the two genders (P-value 0.000). None of the male students and 53.3% of the female in Rabak excreted UI more than 10 µg/dl, whereas 46.9% of the male and 3.3% of the female excreted UI less than 2 µg/dl (fig. 3.4).

In Jabal Awlia the median urinary iodine excretion was 1.10 µg/dl. It was lower in male which was 1.125 µg/dl than that in female which was 1.035 µg/dl without significant difference (P-value 0.266) (Table 3.5 and fig. 3.5). Fig 3.6 illustrates that 73.3% of the male and 81.8% of the female students in Jabal Awlia excreted UI less than 2 µg/dl, while 3.3% of the male and 4.5% of the female excreted UI more than 10 µg/dl.

Table 3.7 shows the median urinary iodine excretion in Elfetihab 2.60 µg/dl. There was no significant difference in median urinary iodine excretion between the male which was 1.79 µg/dl and the female which was 3.56 µg/dl with P-value 0.975 (fig. 3.7). 50% of the male and 43.1% of the female in Elfetihab excreted UI less than 2 µg/dl, while 21.2% of the male and 23.1% of the female excreted UI more than 10 µg/dl (fig 3.8).

Generally the median urinary iodine excretion was low in the four areas. Figure 3.9 shows that the median UIE was the highest in Rabak compared with other areas. This strengthens by the highest iodine content in the tap water in Rabak. In Elfetihab it was higher than Kosti and Jabal Awlia. It was comparable in Kosti and Jabal Awlia.

Table 3.9, 3.10 and 3.11 and figure 3.9,10 and 3.11 illustrate the median urinary iodine excretion of overall samples which was 1.30 µg/dl. There was no significant difference (P-value 0.039) between the median urinary iodine excretion of the male and the female. It was lower in male 1.265 µg/dl than that in the female 1.70 µg/dl.

Table 3.12and 3.13 and figure 3.12 illustrate that the majority of the subjects (83.5%), 11.8% of the male and 20.6% of the female excreted urinary iodine more than 10 µg/dl, while 56.6% of the male and 52.9% of the whole female excreted UI less than 2 µg/dl.
Table (3-1): Median urinary iodine excretion µg/dl in Kosti

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>22</td>
<td>0.63</td>
<td>12.13</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>0.5</td>
<td>1.83</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>0.54</td>
<td>7.79</td>
</tr>
</tbody>
</table>

$t = 2.574 \quad P-Value = 0.013$

Figure 3.1: Median urinary iodine excretion µg/dl in Kosti
Table 3.2: Frequency of distribution of urinary iodine excretion in Kosti

<table>
<thead>
<tr>
<th>CON</th>
<th>Male No.</th>
<th>Male %</th>
<th>Female No.</th>
<th>Female %</th>
<th>Total No.</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>14</td>
<td>63.6%</td>
<td>35</td>
<td>92.1%</td>
<td>49</td>
<td>81.7%</td>
</tr>
<tr>
<td>2-5</td>
<td>1</td>
<td>4.5%</td>
<td></td>
<td></td>
<td>1</td>
<td>1.7%</td>
</tr>
<tr>
<td>5-10</td>
<td>3</td>
<td>13.6%</td>
<td>3</td>
<td>7.9%</td>
<td>6</td>
<td>10.0%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>4</td>
<td>18.2%</td>
<td></td>
<td></td>
<td>4</td>
<td>6.7%</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>100.0%</td>
<td>38</td>
<td>100.0%</td>
<td>60</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Figure 3.2: Frequency of distribution of urinary iodine excretion in Kosti
Table 3.3: Median urinary iodine excretion $\mu$g/dl in Rabak

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>32</td>
<td>2.85</td>
<td>2.81</td>
</tr>
<tr>
<td>Female</td>
<td>30</td>
<td>11.03</td>
<td>18.66</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>5.66</td>
<td>15.03</td>
</tr>
</tbody>
</table>

$t = -4.465 \quad P\text{-Value} = 0.000$
Figure 3.3: Median urinary iodine excretion µg/dl in Rabak

Table 3.4: Frequency of distribution of urinary iodine excretion in Rabak

<table>
<thead>
<tr>
<th>CON</th>
<th>Male</th>
<th>%</th>
<th>Female</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>15</td>
<td>46.9%</td>
<td>1</td>
<td>3.3%</td>
<td>16</td>
<td>25.8%</td>
</tr>
<tr>
<td>2-5</td>
<td>8</td>
<td>25.0%</td>
<td>4</td>
<td>13.3%</td>
<td>12</td>
<td>19.4%</td>
</tr>
<tr>
<td>5-10</td>
<td>9</td>
<td>28.1%</td>
<td>9</td>
<td>30.0%</td>
<td>18</td>
<td>29.0%</td>
</tr>
<tr>
<td>&gt;10</td>
<td></td>
<td></td>
<td>16</td>
<td>53.3%</td>
<td>16</td>
<td>25.8%</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>100.0%</td>
<td>30</td>
<td>100.0%</td>
<td>62</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
Figure 3.4: Frequency of distribution of urinary iodine excretion in Rabak
Table 3.5: Median urinary iodine excretion µg/dl in Jabal Awlia

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>30</td>
<td>1.125</td>
<td>2.17</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>1.035</td>
<td>17.57</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>1.1</td>
<td>11.53</td>
</tr>
</tbody>
</table>

\[ t= -1.125 \quad P-Value = 0.266 \]

Figure 3.5: Median urinary iodine excretion µg/dl in Jabal Awlia
### Table 3.6: Frequency of distribution of urinary iodine excretion in Jabal Awlia

<table>
<thead>
<tr>
<th>CON</th>
<th>SEX</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>0-2</td>
<td>22</td>
<td>73.3%</td>
<td>18</td>
<td>81.8%</td>
</tr>
<tr>
<td>2-5</td>
<td>6</td>
<td>20.0%</td>
<td>1</td>
<td>4.5%</td>
</tr>
<tr>
<td>5-10</td>
<td>1</td>
<td>3.3%</td>
<td>2</td>
<td>9.1%</td>
</tr>
<tr>
<td>&gt;10</td>
<td>1</td>
<td>3.3%</td>
<td>1</td>
<td>4.5%</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100.0%</td>
<td>22</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

### Figure 3.6: Frequency of distribution of urinary iodine excretion in Jabal Awlia
Table 3.7: Median urinary iodine excretion µg/dl in Elfetihab

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>52</td>
<td>1.795</td>
<td>9.12</td>
</tr>
<tr>
<td>Female</td>
<td>65</td>
<td>3.560</td>
<td>7.77</td>
</tr>
<tr>
<td>Total</td>
<td>117</td>
<td>2.600</td>
<td>8.36</td>
</tr>
</tbody>
</table>

\[ t = -0.031 \quad P-Value = 0.975 \]

Figure 3.7: Median urinary iodine excretion µg/dl in Elfetihab
Median urinary iodine concentration µg/dl
Table 3.8: Frequency of distribution of urinary iodine excretion in Elfitaihab

<table>
<thead>
<tr>
<th>CON</th>
<th>SEX</th>
<th>Male</th>
<th>%</th>
<th>Female</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td></td>
<td>26</td>
<td>50.0%</td>
<td>28</td>
<td>43.1%</td>
<td>54</td>
<td>46.2%</td>
</tr>
<tr>
<td>2-5</td>
<td></td>
<td>7</td>
<td>13.5%</td>
<td>5</td>
<td>7.7%</td>
<td>12</td>
<td>10.3%</td>
</tr>
<tr>
<td>5-10</td>
<td></td>
<td>8</td>
<td>15.4%</td>
<td>17</td>
<td>26.2%</td>
<td>25</td>
<td>21.4%</td>
</tr>
<tr>
<td>&gt;10</td>
<td></td>
<td>11</td>
<td>21.2%</td>
<td>15</td>
<td>23.1%</td>
<td>26</td>
<td>22.2%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>52</td>
<td>100.0%</td>
<td>65</td>
<td>100.0%</td>
<td>117</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
Figure 3.8: Frequency of distribution of urinary iodine excretion in Elfetihab

Table 3.9: Median urinary iodine excretion $\mu$g/dl in the four areas around the White Nile

<table>
<thead>
<tr>
<th>Area</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kosti</td>
<td>60</td>
<td>0.54</td>
<td>7.79</td>
</tr>
<tr>
<td>Rabak</td>
<td>62</td>
<td>5.66</td>
<td>15.03</td>
</tr>
<tr>
<td>Jabal Awlia</td>
<td>52</td>
<td>1.10</td>
<td>11.54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>----</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Elfetihab</td>
<td>117</td>
<td>2.60</td>
<td>8.36</td>
</tr>
<tr>
<td>Total</td>
<td>291</td>
<td>1.30</td>
<td>10.91</td>
</tr>
</tbody>
</table>

$F = 6.582$ \hspace{2cm} $P-Value = 0.000$
Figure 3.9: Median urinary iodine excretion $\mu$g/dl in the four areas around the White Nile
Table 3.10: Median urinary iodine excretion $\mu g/dl$ in the four areas around the White Nile in male and female

<table>
<thead>
<tr>
<th>Kosti</th>
<th>Rabak</th>
<th>Gabal Awlia</th>
<th>Elfitaihab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Median</td>
<td>0.63</td>
<td>0.5</td>
<td>2.85</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>12.13</td>
<td>1.83</td>
<td>2.81</td>
</tr>
</tbody>
</table>
Figure 3.10: Median urinary iodine excretion µg/dl in the four areas around the Whit Nile in male and female

Table 3.11: Median urinary iodine excretion µg/dl in the four areas around the White Nile

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>Median</th>
<th>Std deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>136</td>
<td>1.265</td>
<td>7.84</td>
</tr>
<tr>
<td>Female</td>
<td>155</td>
<td>1.70</td>
<td>12.91</td>
</tr>
<tr>
<td>Total</td>
<td>291</td>
<td>1.3</td>
<td>10.91</td>
</tr>
</tbody>
</table>

\[
t = -0.031 \quad P-Value = 0.039
\]

Figure 3.11: Median urinary iodine excretion µg/dl in the four areas around the White Nile
Median urinary iodine concentration µg/dl

- Male: 1.265 µg/dl
- Female: 1.7 µg/dl
Table 3.12: Frequency of distribution of median urinary iodine excretion in all the study area

<table>
<thead>
<tr>
<th>CON</th>
<th>SEX</th>
<th>Male</th>
<th>%</th>
<th>Female</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>0-2</td>
<td>77</td>
<td>82</td>
<td>56.6%</td>
<td>52.9%</td>
<td>159</td>
<td>54.6%</td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td>22</td>
<td>10</td>
<td>16.2%</td>
<td>6.5%</td>
<td>32</td>
<td>11.0%</td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td>21</td>
<td>31</td>
<td>15.4%</td>
<td>20.0%</td>
<td>52</td>
<td>17.9%</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td>16</td>
<td>32</td>
<td>11.8%</td>
<td>20.6%</td>
<td>48</td>
<td>16.5%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>155</td>
<td>100.0%</td>
<td>100.0%</td>
<td>291</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>
Figure 3.12: Frequency of distribution of urinary iodine excretion in all the study area

[Bar chart showing the distribution of urinary iodine excretion in both males and females across different categories (0-2, 2-5, 5-10, >10).]
Table 3.13: Frequency of distribution of urinary iodine excretion in the four study areas

<table>
<thead>
<tr>
<th>TOWN</th>
<th>CON 0-2</th>
<th>CON 2-5</th>
<th>CON 5-10</th>
<th>CON &gt;10</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Kosti</td>
<td>49</td>
<td>30.8%</td>
<td>1</td>
<td>3.1%</td>
<td>6</td>
</tr>
<tr>
<td>Rabak</td>
<td>16</td>
<td>10.1%</td>
<td>12</td>
<td>37.5%</td>
<td>18</td>
</tr>
<tr>
<td>Gabal Awlia</td>
<td>40</td>
<td>25.2%</td>
<td>7</td>
<td>21.9%</td>
<td>3</td>
</tr>
<tr>
<td>Elfitaihab</td>
<td>54</td>
<td>34.0%</td>
<td>12</td>
<td>37.5%</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>159</td>
<td>100.%</td>
<td>32</td>
<td>100.%</td>
<td>52</td>
</tr>
</tbody>
</table>
The result of water analysis

The water iodine content in the White Nile was declined from Kosti to Elfetihab. The mean ± SD in Kosti, Rabak and Elfetihab was 3.9 ± 0.1 µg/l, 3.0 ± 0.09 µg/l and 2.2 ± 0.1 µg/l respectively. Although the water iodine content in White Nile was higher than that in Blue Nile-Sennar which was 2.8 ± 0.12 µg/l and in Nile River- Dongla which was 1.5 ± 0.07 µg/l (table 3.14 and fig. 3.13 and fig 3.14).

Table 3.15 shows that iodine content in tap water in Kosti was 2.8 ± 1.1 µg/l, in Rabak 2.0 ± 0.60 µg/l while in Elfetihab it varied from 1.0 ± 0.03 µg/l to 2.7 ± 1.05 µg/l. Wells were found to have low iodine content. The mean ± SD in Aasel well- Kosti was 2.0 ± 0.60 µg/l and in Umukkaz well was 0.3 ± 0.05 µg/l. Iodine content in Asalaya Canal water was 1.7 ± 0.11 µg/l (Fig. 3.15).

The results of serum hormones analysis

Table 3.16 shows that the mean T3 in the attendant students from the study area was 0.99 ± 0.32 nmol/l. The mean T3 was lower in male than that in female. It was 0.95 ± 0.34 nmol/l in male and 1.01 ± 0.31 nmol/l in female (fig. 3.16). It was noticed that the mean T4 was 95.8 ± 24.06 nmol/l. figure 3.17 shows that the mean T4 in male (83.61 ± 18.11 nmol/l) was lower than in female (101.46 ± 24.63 nmol/l). The mean TSH in the attendant student was 2.06 ± 0.90 mU/l. The mean TSH in female was lower than that in male. It was 2.24 ± 0.68 mU/l in male and 1.96 ± 0.98 mU/l in female. (fig. 3.18).
Table 3.14: Water iodine content µg/l from different sites in the White Nile, Blue Nile and Nile River

<table>
<thead>
<tr>
<th>Area</th>
<th>N</th>
<th>Mean Iodine Conc. µg/l</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Nile-Kosti</td>
<td>8</td>
<td>3.9</td>
<td>0.10</td>
</tr>
<tr>
<td>White Nile-Rabak</td>
<td>8</td>
<td>3.0</td>
<td>0.09</td>
</tr>
<tr>
<td>White Nile-Elfetihab</td>
<td>8</td>
<td>2.2</td>
<td>0.11</td>
</tr>
<tr>
<td>Blue Nile-Sennar</td>
<td>8</td>
<td>2.8</td>
<td>0.12</td>
</tr>
<tr>
<td>Nile River - Dongla</td>
<td>8</td>
<td>1.5</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Figure 3.13: Water iodine content µg/l from different sites in the White Nile, Blue Nile and Nile River
Figure 3.14: Water iodine content µg/l from different sites in the White Nile
Table 3.15: Drinking water iodine content µg/l from different sites in the study area.

<table>
<thead>
<tr>
<th>Area</th>
<th>Mean Iodine Conc. µg/l</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water</td>
<td>2.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Aasel well</td>
<td>2.0</td>
<td>0.60</td>
</tr>
<tr>
<td>Umukkaz well</td>
<td>0.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Tap water – Rabak</td>
<td>3.5</td>
<td>0.18</td>
</tr>
<tr>
<td>Asalaya Canal</td>
<td>1.7</td>
<td>0.11</td>
</tr>
<tr>
<td>Albank Alagary Tank</td>
<td>1.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Wadalbasheir Tank No. 10</td>
<td>2.7</td>
<td>1.05</td>
</tr>
<tr>
<td>Abuseid Tank</td>
<td>1.9</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Figure 3.15: drinking water iodine content µg/l from different sites in the study area.

Table 3.16: The concentration of thyroid hormones ($T_3$, $T_4$) and TSH in subjects from the study area.

<table>
<thead>
<tr>
<th>Sex</th>
<th>N</th>
<th>$T_3$ (nmol/L) Mean</th>
<th>Std. Deviation</th>
<th>$T_4$ (nmol/L) Mean</th>
<th>Std. Deviation</th>
<th>TSH (mU/L) Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>13</td>
<td>0.95</td>
<td>0.34</td>
<td>83.61</td>
<td>18.11</td>
<td>2.24</td>
<td>0.68</td>
</tr>
<tr>
<td>Female</td>
<td>28</td>
<td>1.01</td>
<td>0.31</td>
<td>101.46</td>
<td>24.63</td>
<td>1.96</td>
<td>0.98</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>0.99</td>
<td>0.32</td>
<td>95.80</td>
<td>24.06</td>
<td>2.06</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Figure 3.16: The concentration of thyroid hormones $T_3$ in male & female in subjects from the study area
Mean T₃ concentration (nmol/L)
The results of iodized salt analysis

The iodine in the HDPE packaging salt was in high concentration at the time of manufacturing. It was 152 ± 7.25 mg/kg, but decrease dramatically after 6 and 12 months it became 27.25 ± 17.93 mg/kg and 4.38 ± 3.25 mg/kg respectively. After 6
months the salt crystallized. The iodine content in the core of crystallized salt was 19.4 ± 11.67 mg/kg (table 3.17 and Fig. 3.19).

Table 3.18 shows the iodine content of the HDPE packaging salt that has been manufacturing before 6 months without opening. The iodine concentration was 114.75 ± 29.56 mg/kg, but after 6 months from opening (after 12 months from manufacturing) the concentration became 29.5 ± 14.75 mg/kg (fig. 3.20).

Table 3.19 shows the concentration of iodine in the LDPE packaging salt which was 82.33 ± 13.19 mg/kg at the time of manufacturing. It declined to 60.0 ± 21.42 mg/kg after 6 months, 48.5 ± 13.66 mg/kg after 12 months and 28.17 ± 12.56 mg/kg after 18 months (fig. 3.21).

Figure 3.22 illustrates comparison between the HDPE packaging salt and the LDPE packaging salt.

Table 3.17: The effect of storage on the high density polyethylene packaging iodized salt

<table>
<thead>
<tr>
<th>Time</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Month</td>
<td>8</td>
<td>152.00</td>
<td>7.25</td>
</tr>
<tr>
<td>6 Months</td>
<td>8</td>
<td>27.25</td>
<td>17.93</td>
</tr>
<tr>
<td>12 Months</td>
<td>8</td>
<td>4.38</td>
<td>3.25</td>
</tr>
<tr>
<td>Core of crystal (6 months)</td>
<td>5</td>
<td>19.40</td>
<td>11.67</td>
</tr>
</tbody>
</table>

Figure 3.19: The effect of storage on the high density polyethylene packaging iodized salt
Table 3.18: The effect of storage on the high density polyethylene packaging iodized salt without opening for 6 months

<table>
<thead>
<tr>
<th>Time</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months</td>
<td>4</td>
<td>114.75</td>
<td>29.56</td>
</tr>
<tr>
<td>12 Months</td>
<td>4</td>
<td>29.5</td>
<td>14.75</td>
</tr>
</tbody>
</table>

Figure 3.20: The effect of storage on the high density polyethylene packaging iodized salt without opening for 6 months
Table 3.19: The effect of storage on the low density polyethylene packaging iodized salt

<table>
<thead>
<tr>
<th>time</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Month</td>
<td>6</td>
<td>82.33</td>
<td>13.19</td>
</tr>
<tr>
<td>6 Months</td>
<td>6</td>
<td>60.00</td>
<td>21.42</td>
</tr>
<tr>
<td>12 Months</td>
<td>6</td>
<td>48.50</td>
<td>13.66</td>
</tr>
<tr>
<td>18 Months</td>
<td>6</td>
<td>28.17</td>
<td>12.56</td>
</tr>
</tbody>
</table>

Figure 3.21: The effect of storage on the low density polyethylene packaging iodized salt
Figure 3.22: The effect different packaging types on the iodized salt
Chapter Four
The Discussion

4. The Discussion
This study was carried out in order to estimate the prevalence of iodine deficiency around the White Nile in Sudan.

Iodine deficiency disorders are still a major public health problem in many countries of the world in spite of the fact that the technology available for their prevention makes the problem the most amenable of the nutritional deficiencies to quick and effective control. The prevention and control of IDD, because of its dramatic impact on the quality of life, productivity and educability of millions, would make a major contribution to the development of countries whose people are at risk of developing IDD (Hetzel, 1987). The concentration of iodine in the urine (UIC) is the prime indicator of a person's nutritional iodine status, it is the primary variable used to measure the success of iodine supplementation in a population. The urinary iodine values from populations are usually not normally distributed, and therefore the median value is used rather than the mean (Umesh et al., 2003).

In the studied areas the median urinary iodine excretion was 1.3 µg/dl which indicates severe iodine deficiency. The detailed investigations showed that the median urinary iodine excretion in less than 2 µg/dl, 2-5 µg/dl, 5-10 µg/dl and above 10 µg/dl is 54.6%, 11.0%, 17.9% and 16.5% respectively. According to Lamberg, (1993) Sever; moderate, mild and optimal iodine deficiency is present when the concentration of iodine in urine is less than 2 µg/dl, 2-5 µg/dl, 5-10 µg/dl and above 10 µg/dl respectively. The median UIE was lower in male (1.265 µg/dl) than in the female (1.7 µg/dl) but without significant difference. These results indicated that the median UIE decreased in this area compared with the data published in the WHO report 1997 in which the median UIE was 7 µg/dl and the population above 10 µg/dl were 31.6 %. This result confirmed the result of Abdel Gafar (2005), which showed high prevalence of goitre (54.7%) in this area.

Our results compared with the results carried out in Brazil on school children by Roberto et al; (1997). In this study of 401 countries studied, they found 4 countries with moderately deficient with median UI of 3.3, 3.4, 2.6 and 4.4 µg/dl respectively, and 116 countries with mildly deficient. The results indicated that iodine deficiency disorder is a global health problem and at least 30% of the countries examined in Brazil are at risk of iodine deficiency disease. If the results compared
with developed countries the median UIE was lower than that in Australia which was 84 µg/dl (Lim et al., 2001).

In Kosti the median UIE was found to be 0.54 µg/dl which is lower than that observed by Eltom et al., (1995) in the same area. In the later study the median UIE was 2.6 µg/dl.

Rabak schoolchildren had the higher median UIE 5.66 µg/dl which mean moderate to mild iodine deficiency. This is probably because Rabak consist of many ethnic inhabitant especially the trader men.

In Jabal Awlia and Elfetihab the median UIE show sever iodine deficiency. It was lower in Jabal Awlia (1.1 µg/dl) than in Elfetihab (2.6 µg/dl). A lot of Jabal Awlia populations are poor or refugees and they could not consumed the iodized salt.

The concentration of iodine in White Nile water declined from Kosti to Rabak to Elfetihab. The mean ± SD was 3.9 ± 0.10 µg/l, 3.0 ± 0.09 µg/l and 2.2 ± 0.11 µg/l respectively. This site of White Nile covered by water hyacinth (*Eicchornia crassipes*). This plant has a well developed root system with a very strong absorption capacity (Chigbo et al., 1982; Eltom 1984). This suggests that the iodine content of the White Nile water may be depleted by this water hyacinth.

Despite that, the concentration of iodine in the White Nile was higher than that in the Blue Nile (2.8 ± 0.12 µg/l) and the Nile River (1.5 ± 0.07µg/l). Generally, the water iodine content in the tap water was low ranged between 3.5 µg/l in Rabak to 0.3 µg/l in Umukkaz well-Kosti. This variation in water iodine content can be compared with the results from a study carried out in Denmark. The authors conclude that large geographical and seasonal variations in iodine concentration were found in different beverages supplying an appreciable part of the iodine in Danish diet. The iodine in tap water varied from 2.1 to 30.2 µg/l. The iodine content was in general highest in the eastern part of Denmark and lowest in the western part (Rasmussen et al., 2000).

According to the Arab Healthy Water Association in their website after analysis of 19 brands of water they decided that water iodine content of 0.12 mg/l or
more indicates that this level is generally accepted as safe concentration. World
Health Organization decided that the water iodine content of 0.2 mg/l is sufficient.

Andersen et al., (2002) conducted a study on food and tap water in East and
West Greenland and found that iodine content of tap water was below 3.3 µg/l for all
towns which indicate the low iodine content in tap water in Greenland.

The mean serum T₃ found to be in the low normal level 0.99 nmol/L. It was
higher in the female (1.01 nmol/L) than that in the male (0.95 nmol/L). The same
finding was observrd in the serum T₄ which was in the low normal level (95.80
nmol/L) and the female serum T₄ was higher than the male. The serum TSH was on
the high normal level (2.06 mU/L). It was lower in the female than the male. These
results insure the tendency to develop hypothyroidism in this area which is
strengthening by the results of urinary iodine excretion. The tendency to develop
goitre in female is higher than that in male which confirm the postulation of Delange
(1974) the prevalence of goitre is higher in girls than in boys.

In our results a decrease in T₄ triggers an inversel y proportional increase in
TSH secretion. This increase is characteristic of adaptation of iodine deficiency
(Larsen, 1982). This was clearly evident in previous studies designed to assess
thyroid function in areas of iodine deficiency. It was found that when iodine was
deficient and long lasting, preferential synthesis and secretion of T₃ at the expense of
T₄ occurred (Barzelatto et al., 1967; Ibbertson et al., 1971; Vagenakis et al., 1973;

Two types of iodized salt were analyzed. One was packaged in high density
polyethylene with slightly yellowish and large crystals. The iodine concentration was
152 µg/kg at manufacturing time. But after storage in the house conditions for six and
twelve months the concentrations decrease to 27.25 µg/kg and 4.38 µg/kg
respectively. Meanwhile the salt crystallizes. The iodine concentration in the crystal
core was 19.4 µg/kg. The same salt when kept intact (without opening); the
concentrations six and twelve months latter were 114.75 µg/kg and 29.5 µg/kg
respectively. The second type of salt which was packaged in low density
polyethylene with fine, white and clean crystals, when analyzed the iodine concentration was 82.33 µg/kg. After six, twelve and eighteen months the concentrations become 60 µg/kg, 48.5 µg/kg and 28.17 µg/kg respectively. This type of salt did not crystallize during storage. These results with agreement with Ranganathan et al., (1999) results who analyzed five type of Indian salt iodized with iodate showed losses of 28-51% after 3 months, 35-52% after 6 months and up to 66% after 12 months. These losses of iodine may be due to high temperature in Sudan and/or high humidity in the household. Diosadyl and his co-workers, (1997) held a study to assess the effect of humidity and packaging materials on the stability of iodine in typical salt samples from countries with tropical and subtropical climates under controlled climatic conditions. They conclude that high humidity resulted in rapid loss of iodine from salt iodized with potassium iodate ranging from 30% to 98% of the original iodine content. They added that packaging affected the levels of moisture contained in the system. The LDPE film provided an excellent moisture barrier and at high humidity the HDPE bags lost its iodine content. Other study conducted by Biber et al., (2002) to know the effect of heating on the iodized salt shows that iodine loss was 41.16% by heating at 200°C up to 24 hours, when the iodized salt heated with oxidized agent iodine loss rose up to 58.46 % in 24 hours.

Unfortunately the result of survey on Sudanese population in 2000 by WHO shows that only small portion of households (2.5 to 12.5%) use iodized salt; another 5 to 12.5% are using both iodized and non iodized salt and majority of households (80 to 95% in various provinces) use non-iodized salt (IDD NEWS 2003). Study conducted on 2880 schoolchildren in Uganda, the proportion of households taking adequately iodized salt was 63.8% and the median urinary iodine was 310 µg/l, whereas 36% of 95 urine samples analyzed in 1991 had urinary iodine below 50 µg/l. Only 5% of the 293 urine samples studied in 1999 had the same urine levels. This represents a considerable improvement in iodine intake, which is confirmed by the fact that 63.8% of the study households consume adequately iodized salt (Gabriel et al., 2002).

The crystallization of salt packaged in HDPE may be due to humidity and/or lack of drying agent. Venkatesh et al., 1995 decided that loss of iodine in potassium
iodide fortified salt can be minimized if the salt is pure (+99.5%) and dry (moisture less than 0.1%). Stabilizing agents such as sodium thiosulfate or dextrose, pH buffering agents such as sodium silicaluminate, silicon dioxide, or magnesium carbonate help prevent loss of iodine from iodized salt. According to Diosadyl and Venkatesh 2002, the impurities, physical characteristics and the extent of processing at the source had a major effect on the stability of salt.

Since levels of salt consumption vary and the amount of iodine lost from salt will depend on climate, packaging materials and storage time, it is not possible to establish a global standard for the quantity of KI or KIO₃ which should be added to salt. Current levels of iodization in different countries vary from 100 parts of iodine per million parts of salt, which corresponds to 170 grams of potassium iodate per ton to 10 ppm iodine, which is equal to 34 grams per ton. Most countries fixed levels around 50 ppm iodine. WHO/UNICEF/ICCIDD recommended that levels of iodine in salt expressed as mg iodine per kg salt (ppm) (Venkatesh et al., 1995).

5. Conclusion

IDD (as indicated by goitre prevalence) is severe around the White Nile in Sudan. This finding confirms a study conducted in this area which show that 54.7% of the study population were suffering from goitre and is substantiated by a median urinary iodine excretion of 291 schoolchildren 1.3 µg/dl and the mean T3, T4 and
TSH were 0.99 nmol/L, 95.80 nmol/L and 2.06 mU/L respectively. The drinking water in the study area was suffering from low iodine content. The majority of the people living in this area consumed unionized salt; although the iodized salts available lose most of its iodine content within twelve months which contrast the two years expiry date that specified by the manufacturers.

**Recommendation**

Based on data of the present study, the following recommendations are suggested:

- A household survey for goitre is needed to detect the presence of familial goitre and to reflect the impact of socioeconomic status on goitre.
- Further studies on larger samples from all educational zones may be needed to confirm the status of iodine deficiency around the White Nile.
- Goitrogenic substances both in diet and in water (such as water hyacinth) should receive more investigations and considered in future studies.
- An iodization program and more vigorous educational efforts is required to combat IDD, for the benefit of coming generations.
- Iodine in iodized salt should be stable throughout the manufacturing and distribution by improved processing, better packaging and storage.
- The package of iodized salt must be entitled with clear manufacturing date and expiry date not exceeding one year.
- Governmental laboratories must monitor iodine losses from local iodized salt continuously under local conditions, of production, climate, packaging and storage.
Chapter Five

The Reference

6. The References


Bourdoux P., Thilly C., Delange F., Ermans M., Belgium (1985); Anew look at old concept in laboratory evaluation of endemic goiter. IDD Newsletter Vol. 1 No. 1 pp 8.


Dillmann WH. (1990); Biochemical basis of thyroid hormone action in the heart. Am J. Med. 88: 626-630.


Gaitan E, Cookey RC, Matthews D, Presson R. (1983); In vitro-measurement of antithyroid compounds and environmental goitrogens


Hetzel BS. (1987); Progress in the prevention and control of iodine deficiency disorders. Lancet, 1:266.


John T and Frints V. (1990); A practical guide to the correction of iodine deficiency. Netherlands.


Johnston TB. (1951); A synopsis of Regional Anatomy. Churchill Livingston London.


Kaplan M. (1992); Assessment of thyroid function during pregnancy. Thyroid 2: 57-61.


Michell Webster (1999); Role and importance of iodine in the body. Cambridge essential health center. A health body is nature’s cure. Layout and designed by R Knight.


Osman AK, Fatah AA. (1981); Factors other than iodine deficiency contributing to the endemicity of goitre in Darfur province (Sudan). J. Human Nutr. 35: 302-309.


Pharoah Pod, Butfield IH, Hetzel BS (1971) Neurological damage to the fetus resulting from sever iodine deficiency. Lancet 1:308-310


Roberto Zonato Esteves, Rui Monteriode, Barros Maciel (1997); Urinary iodine excretion in 16803 Brazilian school children. IDD info UIE.


Soriguer F, Millon MC, Munos R, Mancha et al., (2000); The auditory threshold in a school-age population is related to iodine intake and thyroid function, Thyroid 19: 991-999.


Tkanchev A. V, Ramenskaya E. (1991); Dynamics of hormone and metabolic state in polar inhabitants depend on daylight duration.


Umesh Kapil, Preeti Singh, Priyali Pathak and Charan Singh (2003); Assessment of iodine deficiency disorders in District Bharaptur, Rajasthan. Indian Paediatrics; 40:147-149.


Wolff J. (1972); Methods in investigative and diagnostic endocrinology, the thyroid and biogenic amines. Holland Amst and London. 5-17.


