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Health Consequences of Iodine Deficiency

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العواقب الصحية لنقص اليود

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الملخص: تعتبر اضطرابات نقص اليود من مشاكل الصحة العامة الرئيسية في العالم في الوقت الحالي. ولو أن تأثيرها يكون مخفيا . لكنه يؤثر على نوعية حياة الإنسان بشكل كبير. يحصل نقص اليود نتيجة فقر التربة بذلك العنصر والذي يتسبب بنقص اليود في المنتجات الزراعية . وهذا بدوره يؤدي إلى قلة كمية اليود التي يتناولها الناس . وعندما تكون كمية اليود أقل من المطلوب . لا تستطيع الغدة الدرقية إنتاج الكمية الكافية من هرمون الثايروكسين والذي يكون مسؤولا عن حصول سلسلة من الاضطرابات الوظيفية والتطورية تعرف باضطرابات نقص اليود . ويعتبر نقص اليود سببا رئيسيا لمشاكل التطور الذهني عند الأطفال . وكذلك يؤثر على الوظائف التناسلية ويسبب تدنيا في ذكاء الطفل. كما أن انخفاض اليود أثناء الحمل يسبب خللا في إنتاج هرمون الغدة الدرقية عند ألام والجنين . وقلة وجود الهرمون في دماغ الجنين يؤدي إلى التخلف العقلي . إن تلف الدماغ والتخلف العقلي غير القابل للعلاج يعتبران من أهم الاضطرابات الناتجة عن نقص اليود . ثبت أن تناول الملح الذي يحتوي على اليود يعتبر وسيلة فعالة لمنع حصول اضطرابات نقص اليود .

مفتاح الكلمات : اليود . قدامة . تخلف عقلي.

ABSTRACT Iodine Deficiency Disorders (IDD) are one of the biggest worldwide public health problem of today. Their effect is hidden and profoundly affects the quality of human life. Iodine deficiency occurs when the soil is poor in iodine, causing a low concentration in food products and insufficient iodine intake in the population. When iodine requirements are not met, the thyroid may no longer be able to synthesize sufficient amounts of thyroid hormone. The resulting low-level of thyroid hormones in the blood is the principal factor responsible for the series of functional and developmental abnormalities, collectively referred to as IDD. Iodine deficiency is a significant cause of mental developmental problems in children, including implications on reproductive functions and lowering of IQ levels in school-aged children. The consequence of iodine deficiency during pregnancy is impaired synthesis of thyroid hormones by the mother and the foetus. An insufficient supply of thyroid hormones to the developing brain may result in mental retardation. Brain damage and irreversible mental retardation are the most important disorders induced by iodine deficiency. Daily consumption of salt fortified with iodine is a proven effective strategy for prevention of IDD.

Keywords: Iodine; Cretinism; Mental Retardation.

Iodine is a trace element essential for the synthesis of thyroid hormones, triodothyronine (T_3) and thyroxine (T_4). These hormones regulate the metabolic pattern of most cells and play a vital role in the process of early growth and development of most organs, especially the brain. In humans, the early development of the brain occurs during foetal and early postnatal life.[1] Inadequate intake of iodine leads to insufficient production of these hormones, which adversely affect the muscle, heart, liver, kidney and the developing brain. This results in the disease states collectively known as Iodine Deficiency Disorders (IDD).

MAGNITUDE OF IDD

Iodine Deficiency Disorders are known to be a significant public health problem in 118 countries. At least 1,572 million people worldwide are estimated to be at risk of IDD i.e. those who live in areas where iodine deficiency is prevalent (total goiter rates above 5%), and at least 655 million of these are considered to be affected by goiter.[1, 2] Most of these are in developing countries in Africa, Asia, and Latin America, but large parts of Europe are also vulnerable.[4]

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PHYSIOLOGICAL FUNCTIONS OF IODINE

Iodine is an essential dietary element which is required for the synthesis of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). The T_4 and T_3, which are iodinated molecules of the essential amino acid tyrosine, regulate cellular oxidation and hence affect calorigenesis, thermoregulation, and intermediary metabolism. These hormones are necessary for protein synthesis. They also promote nitrogen retention, glycogenolysis, intestinal absorption of glucose and galactose, as well as lipolysis, and the uptake of glucose by adipocytes.[5]

The healthy human body contains 15-20 mg of iodine, of which about 70-80% is present in the thyroid gland. In a day, 60 µg of circulating iodine needs to be trapped by the thyroid for the adequate supply of T_3 and T_4. To extract this amount of iodine from the circulation, the thyroid daily clears several hundred litres of plasma of its iodine. This work can increase several times over in severely iodine deficient environments. To cope with this increased workload, the thyroid enlarges in size, under the influence of the Thyroid Stimulating Hormone (TSH), secreted from the pituitary gland. This compensatory mechanism, triggered by the hypothalamus to increase TSH secretion from the pituitary, causes remarkable enlargement of the thyroid gland (goiter).[6]

An inadequate dietary intake of iodine leads to insufficient production of thyroid hormones, which affects many parts of the body, particularly muscle, heart, liver, kidney and the developing brain. Inadequate hormone production adversely affects these tissues, resulting in the disease states known collectively as iodine deficiency disorders, or IDD. Dietary iodine deficiency stimulates TSH secretion, which results in thyroid hypertrophy. The enlargement of the thyroid gland due to dietary iodine deficiency is called endemic goiter. Iodine intakes consistently lower than 50 µg /day usually result in goiter. Severe and prolonged iodine deficiency, may lead to a deficient supply of thyroid hormones. This condition is referred to as hypothyroidism.[5]

ETIOLOGY OF IDD

Iodine is one of the essential elements required for normal human growth and development. Its daily per capita requirement is 150 micrograms [Table 1]. Soils from mountain ranges, such as the Himalayas, Alps, and Andes and from areas with frequent flooding, are particularly likely to be iodine deficient. The problem is aggravated by accelerated deforestation and soil erosion. The food grown in iodine deficient regions can never provide enough iodine to the population and live-stock living there. Unlike nutrients such as iron, calcium or vitamins, iodine does not occur naturally in specific foods; rather, it is present in the soil and is ingested through foods grown on that soil. Iodine deficiency results when there is lack of iodine on the earth's crust. Living on the sea coast does not guarantee iodine sufficiency and significant pockets of iodine deficiency have been reported from costal regions in different parts of the world.[7]

Iodine deficiency thus results mainly from geological rather than social and economic conditions. It cannot be eliminated by changing dietary habits or by eating specific kinds of foods grown in the same area. Besides nutritional iodine deficiency, a variety of other environmental, socio-cultural and economic factors operate to aggravate iodine deficiency and related thyroid dysfunctions. These include poverty related protein-energy malnutrition, ingestion of goitrogens through unusual diets (particularly by the poor), bacteriologically contaminated drinking water, as well as bulky, high residue diets, which interfere with the intestinal absorption of iodine.[8]

Several environmental and genetic factors interfere with the processes of thyroxin synthesis leading to goiter formation. The genetic factors, which are rare, mainly affect the enzymes involved in thyroxin synthesis. Environmental factors are amongst the most common factors that interfere in thyroxin synthesis and lead to goiter formation. The most important environmental factors are (i) environmental iodine deficiency and (ii) goitrogens. The most frequent cause of goiter in India and other countries is environmental iodine deficiency. However, there is emerging evidence in different countries of world that goitrogens may play a secondary role in several endemic foci. Goitrogens are chemical substances that occur primarily in plant food. They can occasionally be present in contaminated drinking water. Goitrogens interfere in thyroxin synthesis by inhibiting the enzymes involved in the synthesis of thyroxin.

There is also evidence to show that intensive cropping, resulting in large scale removal of biomass from the soil, as well as widespread use of alkaline fertilizers, rapidly deplete the soil of its iodine content. Since

both intensive cropping and use of alkaline fertilizers are widely practiced in almost all developing the countries, it is not surprising that nutritional iodine deficiency and endemic goiter are seen wherever they are looked for in these regions.[5] The relationship between dietary iodine intake and severity of IDD is shown in Table 2.

METABOLISM OF IODINE IN THE THYROID

Iodine enters the body in the form of iodate or iodide in the water we drink or food we eat; the iodate is converted to iodide in the stomach. The thyroid gland traps and concentrates iodide and uses it in the synthesis and storage of thyroid hormones [Figure 1]. The minimum daily iodine intake needed to maintain normal thyroid function in adults is about 150µg/dl. Iodide is rapidly absorbed from the gastrointestinal tract and distributed to extracellular fluids. But the concentration of iodide in the extracellular fluid is usually low because of the rapid uptake by the thyroid gland and renal clearance. It is estimated that 75% of the iodide taken into the body each day enters the thyroid by active transport. About two-thirds of that is used in hormone synthesis, with the remaining amount released back into the extra cellular fluid. The thyroid gland contains the body's largest pool of iodide, about 8 to 10 mg. Most of this iodide is associated with thyroglobulin, a thyroid hormone precursor and a source of hormone and iodinated tyrosines.

The thyroid produces thyroxine (T_4) and triiodothyronine (T_3). Iodine is an essential component of both T_3 and T_4. These hormones regulate the rate of metabolism and affect physical and mental growth and the rate of function of many other systems in the body. The thyroid is controlled by the hypothalamus and the pituitary gland.

The production of thyroxine and triiodothyronine is regulated by the thyroid-stimulating hormone (TSH), released by the anterior pituitary. TSH production is suppressed when the T_4 levels are high, and vice versa. The TSH production itself is modulated by the thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus.

SOURCES OF DIETARY IODINE

About 90% of iodine intake is obtained from food consumed and the remainder from water. Iodine is available in traces in water, food and common salts. It is very low in the foods grown at high altitudes. Iodine found in sea-water is 0.2 mg per litre. Sea weeds and spongy shells are rich in iodine. The iodine content of common food items is given in Table 3. Rich sources are sea fish, green vegetables and leaves like spinach grown on iodine rich soil. Common sources are milk, meat, and cereals. Common salt fortified with small quantities of sodium or potassium iodate is now compulsorily made available in the market as iodized salt to check goiter. Certain vegetables like cabbage, cauliflower and radish contain glucosinolates (thiogluosides) which are potential goitrogens. Eating too much of these foods inhibits the availability of iodine to the body from the food and thus leads to the development of goiter.

THE DAILY REFERENCE INTAKES OF IODINE

HEALTH CONSEQUENCES OF IODINE DEFICIENCY

Iodine deficiency remains the single greatest cause of preventable brain damage and mental retardation worldwide. Eliminating iodine deficiency is recognized as one of the most achievable of the goals that the 1990 World Summit for Children set for the year 2000.

The most important biological role played by thyroxin is in the early foetal stage of life. It ensures the growth, differentiation and maturation of different organs of the body, and particularly the brain. Iodine deficiency has been identified as the world's major cause of preventable mental retardation. Its severity can vary from mild intellectual blunting to frank cretinism, a condition that includes gross mental retardation, deafmutism, short stature and various other defects. In areas of severe iodine deficiency, the majority of individuals risk some degree of mental impairment. The damage to the developing brain results in individuals poorly equipped to fight disease, learn, work effectively, or reproduce satisfactorily. The spectrum of disorders caused due to iodine deficiency affects all the stages of life, from foetus to adult age [Table 3].[9]

If pregnant women's diets do not contain adequate iodine, the foetus cannot produce enough thyroxin and foetal growth is retarded. Hypothyroid foetuses often perish in the womb and many infants die within a week of birth. The current data on the embryology of the brain suggest that the critical time for the effect of iodine deficiency is mid the second trimester i.e. 14-18 weeks of pregnancy. At this time, neurons of the

Table 1: ***The Daily Reference Intakes (DRI) for Iodine***

Life Stage	Iodine mcg
Infants	
0-6 Months	110
7-12 Months	130
Children	
1-8 Years	90
Males	
9-13 Years	120
14-70 Years	150
> 70 Years	150
Females	
9-13 Years	120
14-18 Years	150
19-70 Years	150
> 70 Years	150
Pregnancy	
< 18 - 50 Years	220
Lactation	
< 18 Years	290
19-30 Years	290
31-50 Years	290

Table 2: ***The Spectrum of Iodine Deficiency Disorders***[7]

Foetus	Abortions
	Stillbirths
	Congenital Anomalies
	Increased Perinatal Mortality
	Increased Infant Mortality
	Neurological Cretinism
	Mental deficiency
	Deaf-mutism
	Spastic diplegia
	Squint
	Myxedematous Cretinism
	Mental deficiency
	Dwarfism
	Psychomotor Defects
Neonate	Neonatal goiter
	Neonatal hypothyroidism
Child and Adolescent	Goiter
	Juvenile hypothyroidism
	Impaired mental function
	Retarded physical development
Adult	Goiter with complications
	Hypothyroidism
	Impaired mental function

cerebral cortex and basal ganglia are formed. It is also the time of formation of the cochlea (10-18 weeks), which is also severely effected in endemic cretinism. A deficit in iodine or thyroid hormones occurring during this critical period of life results in the slowing down of the metabolic activities of all the cells of the foetus and irreversible alterations in the development of brain. The growth and differentiation of the central nervous system are closely related to the presence of iodine and thyroid hormones. Hypothyroidism may lead to cellular hypoplasia and reduced dendritic ramification gemmules and interneuronal connections. Hypothyroid children are intellectually subnormal and may also suffer physical impairment. They lack the aptitudes of normal children of similar age, and are often incapable of completing school. Studies have documented that in areas with an incidence of mild to moderate IDD, IQs of school children are, on average, 10 –12 points below those of children living in areas where there is no iodine deficiency.[10]

Endemic Cretinism

Endemic cretinism is the extreme clinical manifestation of severe hypothyroidism during foetal, neonatal and childhood stages of development. It is characterised by severe and irreversible mental retardation, short stature, deaf-mutism, spastic dysplegia and squints. In early eighties, in many seriously endemic Tarai districts of north India, an average prevalence of 1-2% of cretinism was seen. The situation has improved significantly with the supply of iodized salt and cretins are no longer born.

Cretinism seen in severe endemic areas is predominantly of two types (a) neurological cretinism, where the neurological manifestations of thyroxin deficiency early in life, i.e. hypothyroidism, were confined to the in-utero or neonatal stages. (b) Myxedematous cretinism, where besides having mental retardation, sufferers also have myxoedema and dwarfism. This variant of cretinism is presumably because of continuing hypothyroidism through all phases of life.

Cretinoids

Besides the few children who manifest as cretins in an endemic goiter area, a large number of individuals with lesser degrees of mental retardation, speech and hearing defects, psychomotor retardation, as well as gait defects may be seen. Such individuals are

Table 3: ***Iodine content of food***

Food	Iodine (µg)
Salt, iodized, 1 teaspoonful	400
Haddock, 75g	104 - 145
Bread, regular process, 1 slice	35
Cheese, cottage, 2% fat, 1/2 cup	26 - 71
Shrimp, 75g	21 - 37
Egg, 1	18 - 26
Cheese, cheddar, 30g	5 - 23
Ground beef, 75g, cooked	8

known as cretinoids. The prevalence of cretinoids in severely endemic regions may be ten-fold greater or more than fully manifested cretins.[11]

OTHER SYNDROMES DUE TO FOETAL IODINE DEFICIENCY

There is preliminary scientific evidence suggesting that severe iodine deficiency can lead to foetal wastage such as abortion, still births and congenital abnormalities; however, hard evidence available in this regard is limited.[5]

NEONATAL AND CHILDHOOD HYPOTHYROIDISM

Studies have documented that more than 30% of the goitrous subjects in endemic areas are functionally decompensated and hypothyroid despite the `adaptive' enlargement of the thyroid. Research studies on screening the cord blood of over 20,000 newborns discovered that one out of every 10 newborns from the Tarai regions of Uttar Pradesh were hypothyroid at birth.[12]

ADULT HYPOTHYROIDISM

A large number of goitrous adults in an endemic region can have varying degrees of hypothyroidism leading to a variety of clinical symptomatologies and complications related to hypo-metabolic states. This symptomatology can seriously hamper human energy and work capacity with resultant erosion of the economic productivity of endemic regions.[12]

SITUATION OF IDD IN OMAN AND THE GULF

A study conducted in Oman which included 3,061 school children in the 9-12 years age group revealed that 10% of the population showed signs of goiter grades 1a, 1b and 2. Cases of grade 3 were not seen, and 88.1% of the children did not show goiter.[13]

A study conducted amongst 2,996 children in Bahrain aged 8-11.99 years during 1993-94 , revealed that the total prevalence of goiter was 10 % (9.6 % grade I and 0.4 % Grade II), the median urinary iodine excretion levels was 91 µg per liter.[14] Another national study in Oman conducted in 2004 amongst non-pregnant women (sample size 338, age group 15- 49.99 years) revealed that the median urinary iodine excretion levels was 223 µg per liter.[15]

Table 4: ***Relationship between Iodine intake and IDD***

Nutritional Status	Daily Iodine intake (µg)
Associated with cretinism	20 or less
Associated with goiter	20 - 50
Marginal	50 - 100
Normal	100 - 300
More than normal	300 and above

SITUATION OF IODIZATION OF SALT IN OMAN

Presently, there is no national programme for the control of iodine deficiency disorders in Oman; however, since 1995, there has been legislation/Royal decree, for universal salt iodization in the country.

The percentage of households consuming iodized salt was 61% as per the MOH/UNICEF survey in 1998.[16]

CONCLUSION

Today, iodine deficiency is claimed to be the world's single most significant preventable cause of brain damage and mental retardation. The detrimental effect of iodine deficiency on the mental and physical development of children as well as on the productivity of adults has been recognized. The neurological sequelae of iodine deficiency are mediated by thyroid hormone deficiency. All the basic processes of neurogenesis: cellular proliferation, differentiation, migration and selective cell death are impaired during the major period of brain growth.

In Oman, for the prevention of IDD, there is a need to undertake regular cyclic surveys, every 3 - 5 years, to assess the urinary iodine excretion amongst the school age children along with the level of iodization in salt consumed by them. This data can provide the current status of iodine nutriture and status of universal salt iodization in the country. Also, there is a need to enforce strictly the decree of universal iodization of salt in the country so that the population can have ac-

cess only to iodized salt.

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CME QUIZ

1. What are the three sociocultural and ecological factors that aggravate iodine deficiency in a population?

   i) .....
   ii) .....
   iii) .....

2. Mention some clinical conditions that are induced by iodine deficiency.

   i) .....
   ii) .....
   iii) .....

3. What are physiological mechanisms behind the clinical observation that, in spite of severe iodine deficiency in certain individuals, they have no signs or symptoms of goiter or cretinism?

   i) .....
   ii) .....
   iii) .....

4. What is the duration of transient neonatal hypothyroidism in relation to the severity of iodine deficiency and what factors determine the persistence of hypothyroids in the postnatal period?

   i) .....
   ii) .....
   iii) .....

5. What are therapeutic strategies for the different iodine deficiency disorders?

   i) .....
   ii) .....
   iii) .....