

ROLE OF DIET THERAPY IN THYROID PHYSIOLOGY- A SYSTEMIC REVIEWKaleem Ahmad*¹ and Mohammad Tarik²¹Assistant Professor in Department of Moalejat, Rehbar Ayuvedic and Unani Tibbi Medical College, Bhawanigarh, Sangrur, Punjab, India-148026.²PG Scholar un Department of Moalejat, National Institute of Unani Medicine, Bengalaore-560091.***Corresponding Author: Dr. Kaleem Ahmad**

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ABSTRACT

Thyroid is a largest endocrine gland of the body situated in front of neck and secretes tetraiodothyronine (T₄), triiodothyronone (T₃) and calcitonine. Thyroid hormones have great impact on body physiological function. The normal level of thyroid hormones performs normal physiological function and abnormal level responsible for varieties of clinical manifestations in the body. Numerous number of substances involve in the synthesis, secretion, transport, conversion, and functioning of thyroid hormone that are come from diet. These substances enhance and suppress the functions of thyroid hormones. Therefore, need of a review on thyroid physiology in respect to diet therapy.

KEYWORDS: tetraiodothyronine (T₄), triiodothyronone (T₃) and calcitonine.**INTRODUCTION**

Endocrinology is branch of medical sciences that deal with Glands, Hormones, Neurohormones and their disorders. Endocrine system regulates nutritional, behavioural, and reproductive processes as well as body growth, gut function, cardiovascular function, kidney function and response to any kind of body stress. The Endocrine disorders include hyperactivity and hypo-activity of glands lead to numerous clinical features that may vary from mild to severe or life threatening.^[1] Endocrine disorders are place in categories of Non-communicable diseases (NCDs) which are the major cause of death world widely and 82% premature death in low and lower middle-income countries.^[2] Thyroid is the largest endocrine gland of the body^[3] secretes following hormone triiodothyronone (T₃), tetraiodothyronine (T₄) & Calcitonin and normal level of thyroid hormones is essential for normal physiological function in the body. The hyper-secretion and hypo-secretion lead to diseases presentations of thyroid gland that are hypothyroidism, hyperthyroidism and Goitre.^[4] The clinical manifestation of thyroid illness develop in all over the body like weakness, tremor, dry skin, lethargy, hoarseness of voice, oedema of eyelids, heat or cold intolerance, decrease or increase sweating, oedema on face, memory impairment, alter bowel habit, weight change, loss of hair, anorexia, menstrual disturbance, swelling in the neck, etc.^[4,5] In severe case, complications are bacterial pneumonia, megacolon, myxoedema madness, adrenal crisis, infertility, miscarriage etc.^[6] Management of hypothyroidism usually is replacement of thyroid hormone but it also have adverse effect like

osteoarthritis, atrial fibrillation, MI, GIT intolerance, skin rashes, joint pain, loss of taste, fever, agranulocytosis, iatrogenic thyrotoxicosis, bone mineral loss etc.^[6,7] The hyperthyroidism treated usually by carbimazole that also have certain adverse event like Hepatotoxicity, and congenital abnormalities.^[8,9] Therefore, therapy to reverse thyroid illness required long-term use with numerous adverse events.

The autoimmunity plays a major role to interfere thyroid physiology but diets who introduce numerous chemical substance in the body that are essential or toxic to thyroid tissues also responsible to ill health of thyroid gland. So there are need to identify which diets are beneficial or harmful to thyroid gland to prevent development of thyroid illness up to some extent.

Synthesis of thyroid hormone

Essential raw materials for hormone synthesis are Iodine and Tyrosine and both come from diet and absorb from healthy GIT. Synthesis of thyroid hormone occurs in various stages. Thyroglobulin synthesis is the first stage. Thyroglobulin (Tg) is a valuable protein in thyroid follicle and considered as macromolecular precursor of T₄ and T₃. It is synthesize by endoplasmic reticulum and Golgi body of epithelial cell of follicles and secrets and store into follicular cavity. Thyroglobulin synthesize in molecular form of 12S (330kDa) and more stable 19S (660kDa). Iodide trapping is one of the stage in thyroid hormone synthesis. In this iodide actively transported from blood into follicular cells by sodium-iodide symport pump and from cell to lumen by iodide-chloride

pump. Oxidation of iodide is occurring into follicular cell in the presence of enzyme thyroid peroxidase (TPO). After oxidation iodide converted into iodine necessary to react with Tyrosine lead to formation of hormone. Iodination of tyrosine is process in which iodine slowly combined with tyrosine in thyroglobulin and accelerated by enzyme iodinase. It occurs in several stages to form iodotyrosin residues, MIT and DIT. In coupling reactions, the iodotyrosin residue combines in different way to form hormones. Coupling reaction responsible for to combined one molecule of DIT and MIT react to form Tri-iodothyronine (T3), one molecule of MIT and DIT react to form reverse Tri-iodotyronne (rT3) and two molecule of DIT react to form tetraiodothyronine (T4 or Thyroxine).^[9,10]

REGULATION OF THYROID HORMONES

Hormone synthesis of thyroid gland influences by intra-thyroidal factors (iodide in follicular cells etc.) and extra-thyroidal factors (peptide hormones, Thyroid Stimulating Immunoglobulin etc). Under normal Condition, if very low intake of iodine lead to more T3 formation than T4. In excess of iodide in follicular cells then inhibition of hormone formation initially than after 48 hours return to normal due to decrease iodide-transport system. Excess of iodide also inhibits releasing of T3 & T4. In pathological conditions excess of iodide increases formation of hormones. TSH also stimulates thyroid hormone formation by stimulating the all steps of these hormones synthesis. TSH releases from anterior pituitary in the presence of TRH of Hypothalamus. Peptide hormone occupy at TSH receptors under normal condition. Stress, somatostatin, glucocorticoids, dopamine etc. inhibits and Leptin, alpha-melanocyte stimulating hormone stimulates hypothalamus for secreting TRH. Excess of T3 & T4 also inhibits anterior pituitary and hypothalamus by negative feedback mechanism.^[10,11]

The Thyroid nutrition plan

Thyroid hormones function affected by nutritional status of individual either short term or long term nutrition alteration. Nutrition is the science of food and its relationship to the health. Nutritional status is change rapidly and has significant impact on health due to change in diet and lifestyles because of industrialization, urbanization, economic development and market globalization. Non-communicable diseases (NCDs) are significantly increase in modern world due to change in nutritional status of population that includes obesity, diabetes mellitus, cardiovascular disease (CVD), hypertension and stroke, cancer etc. Therefore, nutrition is the most important modifiable factor for NCDs.^[2]

Thyroid dysfunctions also considered into NCDs and thyroid health significantly affected by nutritional status of individual. So for healthy thyroid function numerous nutrients are essential like selenium, Vitamin D, Iron and Iodine etc. other factors and systems that indirectly affect thyroid health such as liver, digestive

system, malnutrition, starvation etc. when we decrease our calories intake then certain hormone level reduce in the body. Nutrition plans for thyroid health are based on nutrient that helps in to improve blood sugar, thyroid, liver, and digestive function.^[2,12,13]

Food use in thyroid dysfunction

Certain types of foods are beneficial for thyroid gland function that contain following nutrients are^[12,13]

- Iodine
- Selenium
- Iron
- Vitamin A
- Vitamin D
- Zinc
- Copper
- Manganese etc.

1. Iodine

1.1 Iodine metabolism

Key role in the physiology of thyroid gland is Iodine metabolism and it constitutes and regulates function of thyroid hormones. Iodine that comes from outside is efficiently absorbed in the healthy gastrointestinal tract in the form of iodide. Iodide contributes in extracellular fluids only in small percentage than iodine pool found in thyroid gland, RBCs, intraluminal fluid of GIT, saliva, gastric juice etc. of total body iodine. Iodide pool from which the thyroid gland is directly derives their iodine supply and serves as the compartment for exchange of body iodine with exogenous iodine. Removal of iodide from extracellular fluid is through expired air, skin, thyroid and kidney. Daily urinary and faecal excretion of iodine is about 500µg in inorganic form & 12µg or in ganic form respectively. In case of impaired gastrointestinal absorption of iodine e.g. chronic diarrhoea, soybean product consumption, anionic resins such as cholestyramine etc. then fecal excretion of iodine increases. Iodine may be loss through feeding of child by mother that is lactation. Body excreted 90% of iodide and kidney contributes about two thirds of it.^[5,14]

1.2 Iodine containing foods

Iodine is the key nutrients for the formation of thyroid hormone along with the tyrosine amino acid. Body excreted 90% of iodide of daily uptake and kidney contributes about two thirds of it. Diet with deficiency of iodine causes unhealthy thyroid function lead to wide spectrum of illness like hypothyroidism with Goitre. In body to maintain iodine balance, dietary sources have great values. Iodine come not only from foods and from water but also come from medications, diagnostic agents and food additive. Daily intake of dietary iodine varies individual to individual depend on soil, water and food habits of an area. The elementary iodine needed for sufficient thyroid hormone production and eliminate all sign of iodine deficiency is about 60µg/day and 100µg/day respectively. The iodine containing foods are-^[15]

Table No.01

S. No	Food	Verities	Example
1	Meat	Red meat	Beef, lamb, pork, veal, horse
		Poultry	Chicken
		Wild animal	Red deer, rabbit
		Processed meat	Air-dried meat, Hamburger, Ham, salami, sausage
2	Fish	Freshwater	Dace, grayling, hake, pike-perch, trout, whitefish, yellow-perch
		Marine	Cod, dab, salmon, flounder, mackerel, plaice, redfish, scorpion fish, shrimps, sole fish, whiting
3	Eggs		
		Whole	Farm egg
		White	Industrial egg white
		Yolk	Separated yolks from farm eggs
4	Dairy product	Milk	Pasteurized milk, raw milk, dried milk
		Cheese	Blue cheese, cottage cheese, fondue mixture, Feta, French hard cheese, herb cheese, Mascarpone, Swiss hard cheese, Swiss semi-hard cheese, Swiss soft cheese
		Yoghurt and quark	Plain unflavored yoghurt, quark
5	Vegetables and fruits	Fresh fruits	Apple, apricot, avocado, banana, berries (blackberries, blueberries, cherry, citrus fruits (clementine, grapefruit, lime, lemon, nectarine, orange) currants, grape, kiwi, mango, melon, raspberries, strawberries), papaw, peach pear, pineapple, plum
		Nuts	Cashew, hazelnut, nut mix (cashew, peanut, walnut) peanut
		Nightshadesvegetables	Tomato, eggplant, bell peppers (green, yellow and red)
		Fresh vegetables	Asparagus, cauliflower, carrot, corn, cucumber, fennel, green beans, kohlrabi, leek, lentils, onion, peas, radish, red cabbage, sprouting broccoli, pumpkin, zucchini
		Salads	Endive, lamb's lettuce, iceberg lettuce, lettuce, lollo rosso
		Herbs	Basil, chives, marjoram, mint, parsley, rosemary, water cress
		Mushrooms	Boletus, black fungus, champignon, chanterelle, shiitake, truffle
6	Cereals		
		Bread	Brown bread, corn bread, croissant, kernel bread, milk bread, potato bread, roll, White bread, whole meal bread, zwieback
		Breakfast cereals	Plain, high fiber, sweetened, wholegrain
		Baked confection	Biscuit, cakees, cookies
7	Pasta		Durum pasta, Durum pasta with egg, whole meal pasta
8	Potato		Bintje new potatoe
9	Rice		Long grain, brown rice, white rice (8
Pharmaceutical products		saturated solution of potassium iodide, lugol's solution, iodized salt, amiodarone, lopanoate, ipodate, angiographic and CT scan dyes, povidone iodine, kelp tablets, prenatal vitamins, iodinated glycerole	

2. Selenium

The concentration of selenium and iodine low in the soil of central Asian region and most European countries. In plants and animals, its concentration depends on soil composition in a locality. The plant use soil Se (selenium) to synthesize amino acid like selenocysteine and enter in animals including human through food chain. Enzyme deiodinase, convert inactive T4 into active T3, contain selenocysteine in its active centre and activity reduces due Selenium deficiency lead low thyroid function. H₂O₂ is a highly reactive cytotoxic metabolite formed during thyroid hormone regulation

inside the follicular lumen. It may be use for iodination and coupling reaction, which can be radical mediate reaction. H₂O₂ (Hydrogen Peroxide) is produce by Duox (dual oxidase) and utilise by TPO for iodination and coupling in thyroglobullines at the surface of follicular cells that face the colloidal space. Se-dependent GPx (glutathione peroxidise) react with H₂O₂ to generate H₂O. GPx is a type of selenoprotein secreted into follicular lumen from thyrocytes and attached with thyroglobuline by non-covalent bond. The secretion and production of GPx is under negative control of calcium signalling pathways. So, GPx-3 is capable to degrade

excessive H₂O₂ and protect thyroid cells. Selenium Deficiency reduces the activity of GPx and iodine deficiency start accumulation of H₂O₂ in follicular lumen, both are causes necrosis of epithelial tissues and thyroid Gland lead to low thyroid hormone biosynthesis. In animal including human selenium enter into body through food chain. In foods, selenium concentration depends on soil quality, accumulation in plant, climatic factors, method of cultivation, breeding & cooking process. There are following food with selenium element e.g. yeast, Brazil nuts, Garlic, Onion, Fish (Salmon etc.), Meat products (Beef etc.), Poultry (Eggs, Chicken etc.), Milk Dairy products, Bread, Miscellaneous cereals, Oils & fats, Green vegetables, Canned vegetables, Fruits, Nuts etc.^[16,17,18,19]

Iron

Iron (Fe) deficiency occur world widely and about two billion people affected and most commonly young women and children. Iron deficiency along with iodine deficiency impaired thyroid metabolism due to decreasing function of Haeme dependent thyroid peroxidase. Efficacy of iodine therapy enhance by iron supplement in case of iron deficiency anaemia. Studies shows that Iron require for thyrotrophic response, increase T₃ & T₄ and utilization of thyroid hormone. However, how iron work on thyroid metabolism not clear yet. Sources of iron are-^[20]

Table No. 02

S.No	Foods	Verities
1	Meats	Lean beef, lean pork, skinned poultry, shellfish, fish, liver, organ meats
2	Egg	Yolks
3	Dried beans or peas	Pinto, kidney, lima, navy, chickpeas, blackeyed peas, lentils, split peas, green peas
4	Green leafy vegetables	Spinach, kale, collards, beet greens, chard, broccoli
5	Dried fruits	Raisins, prunes, figs, dates, dried peaches, dried apricots
6	Nuts and peanut butter	Cashews, almonds, peanuts butter
7	Grains	Iron fortified cereals (read labels), enriched breads, whole grain breads

3. Zinc (Zn)

Zinc is a trace element as like selenium and essential for normal thyroid physiology, homeostasis etc. Zinc plays a complex function in synthesis and action of thyroid hormone. It helps enzyme deiodinase to convert

thyroxine (T₄) into tri-iodothyronine (T₃). Thyroid hormone binding transcription factor also compose Zinc to bind cysteine. In hypothyroid patient, serum level of Zn is become decrease so foods containing Zinc are help to maintain thyroid physiology.^[13,21]

Table No.03

S.No.	Quantity of Zinc	Food
1	12–882mg/1000 kcal	Lamb, leafy and root vegetables, crustaceans, beef kidney, liver, heart, molluscs etc.
2	4–12mg/1000 kcal	Whole grains, pork, poultry, milk, low-fat cheese, yogurt, eggs, nuts
3	1–5mg/1000 kcal	Fish, fruits, refined cereal products, pastries, biscuits, cakes, puddings, tubers, plantains, sausage, French fries
4	0–2mg/1000 kcal	Fats, oils, butter, cream cheese, sweets, chocolate, soft drinks, alcoholic drinks, sugars, jams, preserves

4. Copper (Cu)

Copper also a trace element as like Zinc and third most rich mineral in human body. It helps in thyroid hormone production and over absorption from blood and requires

to stimulate TSH. In hypothyroid patient, serum level of Copper is become decrease as like Zinc. Diets that are contain copper as constituent beneficial to thyroid physiology.^[13,21]

Table No.04

S.No.	Sources of copper
1	Liver, Beef, Ovsters, Biead, white, Tea beverage, Potato, French fried, Pork, ham, Potato, Bread, whole wheat Soft drink, Fruit flavored drink, Milk, Chicken, Peanut butter Banana, potato, white mashed, Orange juice, Spaghetti, tomato sauce & meat Tomato, Egg noodle, Rice, Chili, Pinto beans, Oatmeal etc.

5. Vitamins

Vitamins are essential organic nutrients require in small quantity in body for normal physiological function. It

cannot be synthesized in the body in sufficient quantity except Vit-D and help to utilize other nutrients. Main source of vitamins are foods especially balance diets.

Vitamins supplements may help to prevent many diseases, enhance vitality and therapeutic effect. There are number of vitamins that impaired thyroid factions. Vitamin D production occurs in body. It regulates calcium and phosphorous homeostasis and also cell proliferation & differentiations. In recent year, study shows that deficiency of vitamin D associated with increased risk of diabetes Mellitus, infectious diseases, atherosclerosis and autoimmune condition like

autoimmune thyroiditis. Thyroid hormone and vitamins D, both act by steroid receptors. There are more than 36 types of cells that have Vitamin D receptors including follicular cells of thyroid glands and produces metabolic effect on skeletal, CVS and reproductive systems. Deficiency of Vitamin D enhances symptoms of hypothyroidism and may correlate with increase level of TSH. So always, search vitamin D level in hypothyroid patient. Sources of vitamins D are ^[22,23,24]

Table No.04

S.No	Type Of Food	Example
1	Animal Foods	Egg, Beef, Fish, Milk, Yoghurt, Cheese, Butter etc.
2	Vegetable Food	Margarine, Soybeans Milk, Spinach, Bean, Mushroom, Broccoli etc.
3	Fruits	Orange, Banana, Papaya, Guava etc.

Oxidative stress is responsible for promotion of thyroid dysfunction including hypothyroidism. Vitamins which have antioxidant properties like Vitamin A, C, E etc. help to maintain thyroid health. Vitamin A, animal study shows that deficiency of retinol responsible for decrease iodine uptake by thyroid, synthesis & secretion thyroid hormone and goitre. So level of TSH increase in patient with low level of Vitamin A. but no study on human regarding hypothyroidism and vitamin A deficiency. In some study, there are a strong correlation and goitre size and vitamin A deficiency. Level of TSH and goitre size reduces by therapy of Vitamin A but no change in thyroid hormone concentration. In human body Vitamin B6 acts as a co-enzyme in more than 100 enzymatic reactions. It is necessary for the formation of neurotransmitters, myelin sheaths, hemoglobin, myoglobin, and the metabolism of homocysteine. Some publication shows a Role of vitamin B6 in thyroid dysfunction. an other Study shows that decrease TRH synthesis in hypothalamus lead to low thyroid function due to vitamin B6 deficiency. ^[22,23,24]

Food Avoid In Thyroid Dysfunction

The foods are composed of chemical Substances, some of them harmful to human body and avoid to use. There are number of edible substances that avoid in thyroid dysfunction are ^[5,12,25,26]

- Cruciferous vegetables
- Soy
- Gluten
- Sugar
- Sulphur containing compound
- Excess of iodine
- Thiocyanate and isothiocyanate
- Smoke
- Goitrin and aliphatic Disulfide
- Flavonoids

1. Cruciferous vegetables

The foods that come from Cruciferae/brassicaceae family like cabbage, turnips, Brussels sprouts, rutabagas, broccoli, cauliflower, bok choy etc. release goitrin that interfere thyroid physiology. ^[12] These above foods, when

intake in high amount, interfering iodination of thyroglobulin and inhibit the absorption of iodine by thyroid gland due to presence of sulfhydryl and thiocyanate compounds. ^[27] Thiocyanate and cyanide inhibits uptake of iodine by their competitive effect. They are not present in free ionic form in uncrushed plant. Thioglucoside hydrolysed by specific enzyme to cynates. Thioglucosides are present in, cabbage, broccoli, tunips, sweded, rapeseed, mustard etc. and cyanogenic glucosides are cassava, beans, linseed, bamboo shoots, sweet potatoes etc. ^[2,28]

2. Soy or Soybean

Soy is a plant of Fabaceae/laguminosae and contain isoflavones that can aggravated hypothyroidism. ^[12,27,29]

3. Gluten

Gluten free diet help to relief clinical features of autoimmune disease including thyroid dysfunction. ^[12] Gluten protein found in wheat, barley, rye etc. and produce gliding during digestion that is similar to transglutaminase. Transglutaminase, an enzyme needs to form chemical bond in the body along with thyroid tissues. The gliding stimulates immune system of the body and attack to the thyroid tissue lead to dysfunction. ^[30]

4. Sulphur containing compound

The elementary sulphur is essential element in both plant and animal including human. It obtains from vegetable diet in the form of methionine and cysteine. Sulphur also found in many plant products like vitamins (thiamine, biotin etc.) and other products. ^[31] The vegetable product having compound of sulphur like thiocyanate and isothiocyanate that inhibit iodide concentration and goitrin interfere in organification lead to reduce production of thyroid hormone. ^[28]

5. Excess of iodine

Thyroid hormone synthesis requires an essential micronutrient that is iodine. ^[32] In few subject excess of iodine intake produces thyroid dysfunction but the mechanism of action not fully understood. Wolf-chaikoff effect is the reduction of iodine organification of thyroid

gland in non-endemic area for short duration, but it persists in some case lead to hypothyroidism and hyperthyroidism. The risk to develop hyperthyroidism in a population is about <1% in the presence of excess iodine due to activation of autonomous part of thyroid gland.^[28] So, the amount of iodine that is more than adequate or excess are responsible for abnormal thyroid functions specially in susceptible individual like populations with recurring thyroid disease, old age, embryos, and neonates.^[32]

6. Smoke

Smoking has their adverse effect on thyroid gland in the presence of nicotine and thiocyanate. It associated with increase risk and severity of autoimmune disorders like Graves disease.^[33] It is responsible for thiocyanate overload that is harmful for thyroid physiology. Neonates of mother who addict with smoke are at high risk of hypothyroidism. Smoking also increase level of TSH, LDL, creatine kinase and prolong deep tendon reflex indicate some association with low thyroid function.^[28]

7. Goitrin and aliphatic Disulfide

The substances that contain goitrin like turnips or Seaweeds and aliphatic disulfide like onion, or garlic are associated with thyroid goitre.^[28] Other substances e.g. Millet, Peaches, Peanuts, Pine Nuts, Strawberries, Spinach, and Cassava root have small levels of goitrogens as well.^[27,31]

8. Flavonoids

Flavonoids are polyphenolic compounds of natural occurring in plant.^[34] Plants that have xylem and phloem contain wide classes of pigments known as flavonoids. Iodine organification is strongly inhibited by millet flavonoids.^[28] Flavonoids can inhibit thyroperoxidase activity, decreasing thyroid hormones levels thus increasing TSH and causing goitre.^[34]

9. Lithium and fluoride

Lithium is used in the management of mania and bipolar disorder. It inhibits the releasing of thyroid hormones, increase quantity of iodide in thyroid gland, inhibits coupling reaction and it associated with Goitre, hypothyroidism and autoimmune diseases.^[35] Drinking water with high-level fluoride is also associated with water. So, the substances that contain Lithium and fluoride are avoided to use in excess amount.^[28]

10. Phenol

The Phenolic compound like dihydroxyphenols, resocinole, hexylresorcinol, hydroquinone, catechol etc. inhibits organification of iodide by TPO (thyroid peroxidase) enzyme result low thyroid function.^[28]

Conflict of Interest

None.

CONCLUSION

Function of thyroid hormones affected by nutritional status of individual either alteration in short term and long-term nutrition. Nutrition is the science of food and its relationship in respect to health. Nutritional status is change rapidly and has significant impact on health due to change in diet and lifestyles because of industrialization, urbanization, economic development and market globalization. Non-communicable diseases (NCDs), including thyroid dysfunction, significantly increased in modern world due to change in nutritional status of population that includes obesity, diabetes mellitus, cardiovascular disease (CVD), hypertension and stroke, cancer etc. So, food that contain likes Iodine Selenium, Iron, Vitamin A, Vitamin D, Zinc, Copper and Manganese etc. are responsible for healthy thyroid while Cruciferous vegetables, Soy, Gluten, Sugar, Sulphur containing compound, Excess of iodine, Thiocyanate and isothiocyanate, Smoke, Goitrin and aliphatic Disulfide and Flavonoids are responsible for ill-health of thyroid.

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