THALASSAEMIA INTERNATIONAL FEDERATION

Nutrition in Thalassaemia

A Guide for Patients, Families and Caregivers

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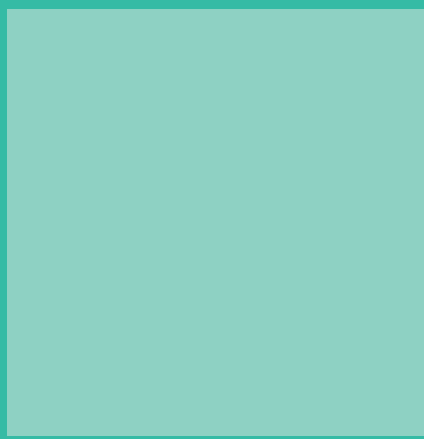

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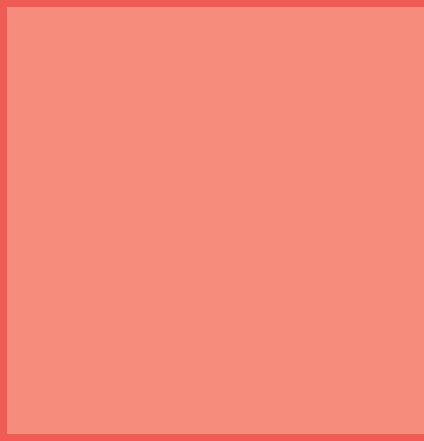

FORWARD

On behalf of the Board of Directors of the Thalassaemia International Federation (TIF), it is my great privilege to write the forward to the 'Nutrition in Thalassaemia. A Guide for Patients, Families and Caregivers'

There is much scattered literature concerning nutrition in the congenital anaemias. These conditions encompass a broader range of nutritional and metabolic effects compared to acquired deficiency anaemias, which primarily focus on correcting the deficiency. In congenital anaemias, factors such as potential nutritional deficiencies, the impact of medications (especially chelating agents), possible nutrient toxicities and benefits, and complications potentially influenced by nutritional factors all play a role. Moreover, organ damage, such as liver damage, can further influence nutritional factors and metabolic effects.

These complex influences can significantly affect daily food intake. Patients seeking guidance have two primary sources of reliable information: a dietician knowledgeable about haemolytic anaemias and ineffective erythropoiesis, or a physician/haematologist well-versed in both anaemias and dietary influences. Unfortunately, both specialists can be difficult to find.

The Thalassaemia International Federation, continuing its tradition of producing guidelines and educational material for healthcare professionals and patients, published the "Nutrition in Thalassaemia & Pyruvate Kinase Deficiency: A Guideline for Clinicians" in 2023. In 2024, the objective was to create a concise reference guide for people living with thalassaemia, their families, and/or caregivers. This new publication provides an overview of nutritional requirements, methods of nutritional assessment, explanations of nutrients of special importance for people living with thalassaemia, and the role of nutrition and diet in managing complications. It concludes with a set of practical recommendations.

TIF extends its gratitude to the two key authors, Dr Ellen Fung, PhD, RD and Dr Anne Yardumian MD, Consultant Haematologist, for their immense contribution. It also acknowledges the support of Dr Michael Angastiniotis (TIF Medical Advisor), Dr Androulla Eleftheriou (TIF Executive Director), and TIF Board Members, Mr. George Constantinou, Ms. Manal Zaatar, and Ms. Maria Hadjidemetriou.

On behalf of the Board of Directors of the Thalassaemia International Federation (TIF)

Panos Englezos
President

1. Introduction

Good nutrition – eating and drinking a broad range of healthy foods, not too little, and not too much! – is important for everyone. This has become increasingly evident over recent years, and the crucial role of a healthy diet for all of us is backed by scientific research. It is important not just for growth and development in young people, but throughout our lives to support our immune system and help us fight infections, keep our bones healthy, manage inflammation and any tissue damage, and reduce our risks of long-term conditions including 'cardiovascular' problems such as heart disease, stroke, and diabetes.

Haemoglobin is the red pigment in blood which carries oxygen from the lungs to the tissues, and adequate levels are essential for life. **For people with conditions such as thalassaemia, who cannot make sufficient amounts, and who may need regular blood transfusions, nutrition is especially important for the following reasons:**

- To ensure adequate intake of essential nutrients, to optimise the functioning of the various body organs, which may be subject to additional challenges because of the condition and its treatment.
- To avoid too much of any nutrient which could be harmful, such as food containing a lot of iron if their iron levels are already high, and alcohol which can cause or worsen any liver inflammation.

At the same time, managing a good and varied diet may be more of a challenge for people with these conditions. At times they may be more fatigued than other people, so that preparing and cooking a nutritious meal may seem like 'a big ask', or they may suffer from side effects of medication, and not feel hungry.

In this short guide, we hope to help affected individuals and their families rise to these challenges, and so to optimise their health and wellbeing. We will also cover some of the assessments that can be offered to check that your nutrition is good, and to monitor progress if you change your diet accordingly. We will then include some details of the specific dietary elements which are important, with guidance about those which are especially important for people with thalassaemia. Finally, we will cover a few common complications - bone thinning or osteoporosis, diabetes mellitus, heart disease, and kidney disease – in which careful dietary management can be particularly helpful.

Much of the content will also apply to people with other hereditary iron-loading anaemias, such as pyruvate kinase deficiency, and Diamond-Blackfan anaemia, and individuals and families affected by these conditions may also find it useful.

You may come across a word or phrase that you are not familiar with; please check the 'Glossary' at the end where we hope you will find it explained.

For brevity, in this guide we have not included specific details about thalassaemia – more information for those who feel they don't know enough about the conditions can be found at TIF's other publications:

https://thalassaemia.org.cy/publications/tif-publications/

2. General nutritional requirements

To maintain health, our bodies need us to consume two broad food categories, called macronutrients and micronutrients. Macronutrients are needed in much larger amounts, while micronutrients are required in smaller quantities. In addition to these specific nutrients, adequate fluid, and fibre intake are also essential – to decrease fatigue and constipation, maintain good circulation and weight maintenance, permit optimal kidney functioning and bowel function, and even promote the body's ability to get rid of iron. While water is the preferred beverage for everyone over 3 years of age, the amount needed will depend on how old you are, how active you are, and how hot it is outside. In general, most adults need a minimum of 8 cups of water per day. Many people don't consume enough fibre: it is suggested that adults consume at least 3 servings of whole grains per day which may include whole grain bread or pasta, oatmeal, or brown rice. Not only are these foods rich in fibre, but they are also packed with lots of B-vitamins, a win-win.

Macronutrients include protein, fat, and carbohydrates. Carbohydrates, sometimes known as 'carbs' are our primary energy source and come from foods like bread, rice, pasta, grains, fruits, and vegetables. Protein plays an important role in body structure and function, regulates cellular and bodily processes, and can provide energy if carbohydrate or fat levels are low. Proteins are available in meat, dairy products, pulses, beans, and grains. Most people consume plenty of protein, but for people who are vegetarians or vegans, the type of protein is also important. Our bodies need 'complete' proteins that have all the essential building blocks (amino acids). Meat, poultry, fish, and dairy are rich in complete protein, but beans, lentils, and nuts have 'incomplete' proteins. Eating a variety of plant-based foods or combining foods with incomplete proteins will lead to 'complete' proteins. Great combinations include rice and beans, hummus and pita bread, or peanut butter on whole wheat bread.

Fat is the primary source of stored energy in the body; fats also play important roles in cell structure and function, temperature regulation, and forming a protective layer around the body's organs. Dietary fat is found naturally in oils, meats, dairy, nuts, and some plants (e.g. avocados). Dietary fat is also abundant in processed foods such as crisps, french fries (chips), and other fried foods. When it comes to fat, the type of fat you eat is more important than the total amount you consume. It's best to choose more foods that have 'good fats', or unsaturated fats (e.g. olive, canola, and sunflower oils, as well as the oils found in nuts and fish) over saturated fats (e.g. the fat found in red meat, butter, and ice cream) and to avoid processed foods with 'trans' fats (e.g. margarine, store bought cookies and cakes, crisps, chips or french fries).

Micronutrients such as vitamins, minerals and trace elements are necessary for supporting metabolic processes – the body needs them for every cell to do its job. They cannot be synthesised in the body in sufficient quantities, and therefore need to be taken regularly in the diet. They include the B vitamins: thiamin (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate (B9), cobalamin (B12), and vitamin C – these are water soluble and usually needed to be ingested often as they are excreted in the urine rather than stored in the body. Fat-soluble vitamins include vitamins A, D, E, and K, and can be stored for longer periods. Minerals required in relatively larger amounts are calcium, magnesium, phosphorus, sodium, potassium, and chloride; relatively tiny amounts are required of the trace elements iron, zinc, copper, iodine, and selenium.

Eating a wide range of foods, especially different fruits, and vegetables, helps our diets to be rich in important vitamins and minerals, and healthy foods come in a variety of colours. Eating foods of many colours is especially good for us and we are encouraged to 'eat around the rainbow'. For example, kale is green, carrots yellow or orange, beets are red, and red cabbage is purple – and each derives its colour from the various antioxidants they contain, and these substances are important for reducing the damage that iron in the body can cause. Be careful however to distinguish between naturally vibrant healthy foods such as these, and processed foods with colour additives like breakfast cereals such as 'Fruit Loops' these processed foods should NOT be considered part of the healthy rainbow!

Eating nutrient-dense, minimally processed foods and drinks, including a variety and balance of fruits, vegetables, grains, and high-quality proteins and fats can, for most people, provide the necessary macronutrients and micronutrients. However, in both children and adults with thalassaemia, nutritional inadequacy can arise for a complex of reasons. Reduced dietary intake, increased excretion and / or raised requirements of nutrients can result in nutritional imbalances and deficiencies. To learn more about these possible problems, please read on!

3. What puts people with thalassaemia conditions at particular risk of nutritional deficiencies?

Of course, as for anyone else, dietary choices for people with these conditions may be limited by availability and affordability or guided by cultural or religious considerations. Overall, inadequate dietary intake is the most obvious reason for nutritional inadequacy and several things which can affect people with thalassaemia may contribute to reduced food intake: stress or depression, fatigue, physical inactivity, or hormonal disturbances such as underactive thyroid or adrenal glands. Severe anaemia is known to contribute to poor appetite, a biological determinant of food intake along with hunger and taste. Although adequate blood transfusions, so that blood levels do not fall too low, are available to most people, this remains an issue for people in some parts of the world.

Reports suggest that energy intake – that is, number of calories consumed - appears to be balanced with energy used in many adults with thalassaemia, yet nutrient density is lacking - that is, their intake may be largely of foods high in calories but limited in nutritional value, leading to poor intake of sufficient micro-nutrients and trace elements. Food diaries suggest that some people, anxious about adding to their iron levels through their diet, exclude otherwise healthy, iron-containing plant-based foods like spinach, beans, legumes, lentils, and whole grains in favour of higher-calorie, nutrient poor, 'filler' foods.

When haemoglobin levels fall before transfusion, the bone marrow where the blood cells are made increases its activity in an attempt to correct this. At these times, there are increased requirements for some vitamins including folic acid, protein and zinc; these increased demands need to be matched by dietary intake or supplements [see later]. The increased demand may be present at all times for people with milder forms of thalassaemia, who do not require regular transfusions. Similarly, calorie (energy) requirements may be increased before transfusion, and for people with thalassaemia who are not on regular transfusions.

Another way in which adequate nutrition may be challenged is if absorption of foodstuffs from the gut is reduced: in thalassaemia however, it does not seem that general absorption is disturbed. The exception is for people who have iron damage to the pancreas causing reduced output of the enzymes necessary to break down and digest your food before you absorb its nutrients; these people need to take some enzyme supplements such as Creon or Pancrex at mealtimes.

Tea is frequently consumed at mealtimes by adults with thalassaemia, as it reduces absorption of iron from the food. However, when tea is given to young children instead of milk at meals, it reduces their intake of calories, protein, calcium, zinc, and other essential nutrients found in abundance in milk.

Many people with thalassaemia, especially those receiving regular transfusions, have to take medication to help the body get rid of extra iron: iron chelators. For some, nausea or other stomach or bowel complaints accompany the use of these medications such as deferiprone and deferasirox; such symptoms can lead to some missed meals, food intolerance and decreased or altered food intake. Also, essential trace minerals may be lost along with iron during chelation therapy, increasing the requirement for these minerals. Especially when liver iron levels are near normal, chelator treatment can result in loss of zinc and copper as well as iron. On the other hand, people with thalassaemia who have significant iron overload have increased needs for certain nutrients, in particular the antioxidants (vitamins C, E, selenium, and zinc; see later).

Finally, although 'following doctor's orders' for medical care, transfusion regimens and medication use is critical to maintaining health in people with thalassaemia, time spent focused on health maintenance may borrow from time spent in planning for meals, food shopping and meal preparation; added to fatigue from anaemia or gastrointestinal stress from medications, the energy and motivation required for these tasks may sometimes be lacking.

4. Nutritional assessments

Knowing how your nutrition can be assessed may be of interest, and this section might be helpful towards discussions with your health-carers, about what tests you might need or have had, and your results. Nutrition assessment is as simple as following the A, B, C and Ds.

A. 'Anthropometric' or simple body measurements

These include height and weight, and calculation of 'body mass index' [your weight in kg divided by height in metres squared. For children and young people who are still growing, height and weight should be put on a graph – or 'centile chart' - which shows the normal ranges for boys and girls of their age. Measurement around certain parts of the body, for example, around the upper arm, and assessing the amount of fat under the skin using a skin-fold measuring tool can also give useful information.

These may be supplemented by a more detailed study of the fat and muscle mass in the body. From early teens at least, a regular scan called DXA scan (sometimes known as DEXA) is commonly undertaken to check on bone density (bone health). Body fat and body composition can be assessed by DXA at the same time.

B. Biochemical assessments

The results of routine blood tests form the basis for managing these conditions, and blood samples are taken at most if not all appointments. As well as measuring haemoglobin levels and other blood cell numbers, and checking on kidney and liver function, tests routinely measure the levels of calcium, iron, and zinc and of some vitamins including folate and vitamin D. Additional tests may be undertaken less frequently, or if there are any concerns about nutritional status, and urine tests – for example checking calcium output – can give extra information when needed. The results of all these tests can guide as to the adequacy of dietary intake, and the possible need for extra amounts in the form of supplements.

C. Clinical assessments

Inadequate nutrition is just one of the causes which can result in reduced growth rates in children and teenagers. Others include chronic anaemia, liver disease, reduction in growth hormone, thyroid gland activity, or puberty hormone levels. Faltering growth in children, or delayed development, or being underweight in adults, should be picked up on routine monitoring at clinic appointments – through the assessment types A and B described above. Examination of children for signs of pubertal development should be undertaken routinely, at least yearly, from the age of 10.

Other visible signs of possible nutritional deficiency only usually appear in cases of severe undernutrition, but can include hair loss, changes in hair colour, fluid swelling of the ankles, skin lesions, bleeding gums, fatigue, poor concentration, or decreased appetite.

D. Dietary assessments

Assessment of dietary intake is the final essential step in the comprehensive nutritional status assessment. This is a complicated process, which should be undertaken by a qualified nutrition professional. 'Food diaries' are often used, where the nutritionist asks the individual, or family members for children, to record everything they eat and drink over a period, ranging from 1 day to 7 days. Obtaining accurate dietary intake of school-aged children and teenagers can be especially difficult as they may consume the majority of their meals and snacks outside the home, and questions regarding cultural food restrictions and availability also need to be considered. Once dietary information has been obtained, it is quantified using a dietary analysis tool, and compared to reference data from healthy individuals. Understanding an individual's food and preferences and restrictions is key to personalising nutrition recommendations for them.

5. Nutrients of special importance

There are many important nutrients, vitamins, and minerals, in the food we eat every day. For most people, consuming a varied, nutrient-dense diet, that is also rich in whole grains, fruits, and vegetables with limited amounts of added sugars is sufficient for optimal health. However, for people with thalassaemia, it may not be sufficient just to eat a varied diet, and additional dietary supplements may be necessary. The vitamins and minerals for which people with thalassaemia are often deficient are described here, along with which additional dietary supplements may be beneficial. We talk a bit about each here, listed in alphabetical order rather than order of importance!

Calcium

Calcium, an essential mineral in our diet, is crucial for healthy bones and teeth. Small amounts of calcium are also needed for muscles to work, blood to clot and nerves and hormones to function correctly. Given many people with thalassaemia have some bone weakening, calcium is of particular importance. Unfortunately, calcium intake is often inadequate. It is found naturally in abundance in dairy products, milk, yogurt, and cheese. People who are intolerant of lactose must limit their intake

of dairy products and therefore may have poor calcium intake. Some green vegetables (kale, broccoli) and tofu are also rich sources of calcium. However, the calcium found in high concentrations in spinach is poorly absorbed. Vitamin D is essential for calcium absorption from food. Adults with sufficient stores of vitamin D need at least 500 mg of calcium per day. A diet rich in calcium is preferred over 'extra' calcium in the form of supplements, to reduce the risk of kidney stones.

If calcium supplements are used to enhance intake, it is recommended not to take more than 500 mg/day. There are 2 main types of calcium supplements, calcium carbonate (40% calcium) and calcium citrate (~ 20% calcium). Consider cost, form (chewable, tablet) and absorbability, before deciding on a supplement that works best for you. As an example, a 1250 mg calcium carbonate supplement contains 500 mg of calcium, while a 1000 mg calcium citrate supplement only has about 200 mg of calcium. Calcium carbonate supplements should be taken with food for best absorption, while a calcium citrate capsule can be taken with or without food. Calcium supplements that also contain vitamin D are preferred.

Folate

Folate, also called folic acid, is a water-soluble vitamin, so if you consume too much of it, your body can get rid of it easily. Folate is found in dark green leafy vegetables, brussels sprouts, beans, and peas. In some countries, folate is also added to breads, grains, pasta, and cereals. Folate is important for helping cells to divide; it is particularly important for pregnant women to get plenty of folate. Because people with thalassaemia have a high turnover of red blood cells, more folate is needed, and supplementation is typically necessary for non-transfusion dependent patients. A diet rich in foods containing folate is encouraged for all, while additional supplementation with 1 mg/day or 5 mg/week of folic acid is recommended for most people with non-transfusion dependent thalassaemia.

Iron

Of course, this is the 'trace metal' which is discussed most in relation to thalassaemia and its care. This is because build-up of extra iron in the body is one of the big problems for people with the condition: iron is absorbed from the gut in larger amounts, and every time you have a blood transfusion additional iron enters the body. While iron is essential for making red blood cells, proper muscle functioning, and several other chemical processes in the body, too much is harmful. There is no way for the body to get rid of excess iron, so it builds up and is deposited in various internal organs, and above a certain level it causes damage by inducing what is known as 'oxidative stress'. The liver, heart, and endocrine glands are the organs which mostly suffer from iron damage.

People who are receiving regular blood transfusions are at highest risk of iron build-up, but those who receive only occasional or even no transfusion can still gradually accumulate too much iron through dietary absorption which can also be damaging to the body. Iron levels are usually monitored using the level of ferritin in the blood; the normal range is ~15-300 ng/ml but ferritin can easily rise to 1,000 ng/ml or more and at this sort of level your medical team will usually recommend to you one or other of the medications used to remove iron from the body, the so-called iron chelators. Iron levels are often checked too using magnetic resonance scans which can accurately measure the amounts of iron in the heart and liver.

For people who are receiving transfusions and are on regular chelation treatment, with iron levels being closely watched, the amount of iron absorbed from the diet is not going to add much, and so careful avoidance of iron-rich food is not so important.

In those with milder forms of thalassaemia who are on only rarely or never transfused, the contribution of iron in the diet is greater, and therefore limiting the amount of red meat and other high iron foods and iron-fortified foods such as breakfast cereals in the diet is recommended.

Many people also choose to drink tea with meals as there is evidence that this can reduce the amount of iron absorbed from meals. However, this is not good guidance for children, who otherwise often drink milk which is a much better general nutrient and rich source of calcium; drinking this instead should be encouraged.

Vitamin C

Vitamin C, also called ascorbate or ascorbic acid, is a vitamin found in citrus fruits (oranges, grapefruit, lemons), strawberries, bell peppers, tomatoes and even baked potatoes. It is an antioxidant, that means it protects the body from oxidative stress, which can lead to tissue damage. Vitamin C is also important for wound healing, it helps the body absorb iron from food, and helps chelator medications remove iron from the body. People with thalassaemia have lots of iron in their body, and risk of tissue damage due to oxidative stress, therefore they often need

more vitamin C. Vitamin C supplementation may help chelator medications work better, but taking vitamin C without chelation can be dangerous. For people with lots of body iron, it is important to talk with a doctor before starting any supplementation. For people who do not need transfusion regularly, it is best to avoid eating vitamin C-rich foods (e.g. tomatoes, oranges) with plant-based foods that have a lot of iron (e.g. beans, fortified cereals) as iron absorption will increase.

Vitamin D

Vitamin D is unusual in that it is an essential fat-soluble vitamin found in our diet, but it can also be synthesised in our skin after exposure to the sun. Vitamin D is found naturally in only a few foods including fatty fishes (e.g. sardines, salmon, swordfish), fish oils (e.g. cod liver oil), wild mushrooms and egg yolks. Given how common vitamin D deficiency is, some countries (Finland, Norway, Sweden, Canada, and the US) add vitamin D to foods, such as milk, cereals, yoghurt, and orange juice. Vitamin D is important to strengthen bones and help them grow, it helps the body absorb calcium, and is important for our immune systems to fight infection. Vitamin D along with calcium, can protect against osteoporosis or bone thinning, which is common in people with thalassaemia. It is difficult to get the amount of vitamin D needed from food alone, therefore extra in the form of supplementation is often recommended. Either vitamin D2 (also called ergocalciferol) or vitamin D3 (also called cholecalciferol) taken by mouth is recommended at a

dose of 1,000 to 2,000 IU/day or 50,000 IU per month in adults. Your health-carers may also recommend that you include vitamin K or magnesium along with vitamin D supplementation, to assist with vitamin D function. As vitamin D can be toxic in very high doses, it is also recommended to have the level of vitamin D in your blood assessed every 6 months to maintain a circulating level, measured as '25-OH vitamin D', between 30 – 50 ng/mL.

Vitamin E

Vitamin E, another essential fat-soluble vitamin, works in tandem with vitamin C to protect the body against oxidative stress. It is found naturally in vegetable oils, nuts, and nut butters as well as wheat germ. Though it is not routinely tested in many clinics, research studies suggest that people with thalassaemia may be at risk for deficiency. Vitamin E supplementation may be useful especially to those with elevated liver iron. Annual assessment of vitamin E in the blood is recommended, and supplementation provided to those with deficiency.

Zinc

Zinc is important for good immunity against infections, growth, pubertal development, bone health and may also decrease the risk of developing diabetes. It is found in many protein-rich foods including beef, chicken, beans, yoghurt, and cheese. Interestingly, oysters are a particularly rich source of zinc, for those that can get them and like them! People with thalassaemia are often deficient in zinc, particularly those on chelator medications and those with increased liver iron. Scientific research suggests that zinc supplementation may improve growth in children, as well as bone health and glucose control in adults with thalassaemia. Annual assessment of zinc in the blood is recommended and supplementation with 25 mg per day provided to those who are deficient. If zinc supplementation is recommended, formulations without sulfate (e.g. zinc citrate, acetate, gluconate) may be gentler on the stomach.

Tea, Botanicals/Other Supplements

- Drinking tea, either black or green, with meals can decrease iron absorption and may be of benefit for patients with non-transfusion dependent thalassaemia.
- Botanicals such as turmeric, wheatgrass and silymarin may have some benefits in reducing iron toxicity and protecting the liver. Talk with your doctor before starting on any new supplement.
- Supplementation of any kind should not take the place of a varied diet that is rich in fruits and vegetables.

6. Complications in which nutrition and diet have special importance

Osteoporosis

Osteoporosis, or thinning bones, is the condition in which the bones are weak and more likely to fracture. It is often called a "silent disease" because it slowly develops from childhood and an individual may not know they have weak bones until they suffer a fracture. Osteoporosis is the most common problem in adults with thalassaemia, affecting more than half of people who are transfusion dependent, even if they are receiving good transfusion and chelation regimens. Along with the increased risk of fracture, many people also have chronic bone pain especially in the spine, which can impact quality of life.

People with thalassaemia are at particular risk for developing osteoporosis due to changes in the bone marrow, low sex hormone levels, iron overload, use of chelator medications, inactivity, increased losses of calcium in the urine, as well as low levels of vitamin D and zinc. Optimising vitamin D and zinc in your diet is important, as is ensuring you take in adequate magnesium and vitamin K, which help your body use calcium and vitamin D to strengthen your bones. Low levels of magnesium are a risk factor for bone thinning, and it is important to have levels checked, and to correct levels by increasing dietary intake (see food sources in glossary) or taking supplements.

For people who have sustained a fracture, they are at increased risk of fracturing again. The best way to decrease the risk of osteoporosis and fracture is to build strong bones in childhood and adolescence, though optimising nutrition and physical activity can be helpful at any age.

It is recommended that people have a bone density test (DXA or DEXA scan) to assess how strong their bones are, starting in childhood or adolescence and then every 1 to 2 years. This will help their team to advise if additional treatments are needed. People with thalassaemia can take an active role in promoting bone health by:

- Participate regularly in physical activity, particularly 'weight bearing' activities such as walking, jogging, dancing, and jumping. 'Weight-less' activities such as swimming and biking are also important for heart health but are less helpful for bone health. It is especially important for children to be active.
- Encourage activities that improve flexibility such as yoga and Pilates. These types of exercises improve muscle strength and balance, thereby reducing the risk of falling.
- Consume adequate amounts of calcium particularly from food (e.g. milk, yogurt, tofu, kale). If a calcium supplement is taken, don't take more than 500 mg/day
- Take a vitamin D supplement of 1,000 – 2,000 IU/day or 50,000 IU per month.
- Have zinc blood level checked. If it is low, take a zinc supplement at a dose of 25 mg/day or 50 mg every other day.

Your medical team may also discuss with you the possibility of taking extra medications to help strengthen your bones if they are found to be thin as per your country's national guidelines.

Diabetes mellitus

Diabetes mellitus, usually just called 'diabetes', is the condition in which the body's ability to handle sugars is impaired, leading to high blood glucose levels. The hormone insulin, produced by glands in the pancreas, is a key mechanism by which we normally control blood sugar levels. Diabetes is common in people with thalassaemia, largely due to iron damaging the pancreas, and so reducing insulin production. Liver inflammation can also lower insulin's effectiveness and contribute to impaired glucose tolerance.

Patients with thalassaemia and diabetes require a coordinated care plan drawn up with their haematologist, diabetes specialist and dietitian, to ensure they maintain adequate nutrition according to their individual needs, while supporting optimal glucose control. They require focused nutritional education, with coordinated meal and snack planning, and medication offered for diabetes – including insulin or tablet medication to help control sugar levels – needs to be considered and planned alongside their other medication such as iron chelation.

Lifestyle and dietary advice for people with thalassaemia and diabetes include:

- NO cigarette smoking!
- Exercise regularly, such as brisk walking, as long as heart checks show this is safe for the person.
- Consume small, regular meals, spread over the day.
- Choose carbohydrate foods that are high in dietary fibre, such as wholegrain breads and cereals, beans, peas, lentils, brown rice, and oats.
- Avoid large portions of starchy carbohydrates that are low in fibre (high glycaemic index), such as potatoes, white bread, white rice, and pasta.
- Consume fruit and vegetables every day.
- Use small amounts of fats and oils in cooking. When using oils, choose olive oil and rapeseed oil (canola oil) instead of palm or coconut oil.
- Consume fewer fried foods and cut fat off all meat, preferring less fatty meats, such as chicken or turkey.
- Avoid large amounts of saturated fats, such as butter, lard, ghee, red palm oil, pastry, cheese, crisps, mayonnaise, and cakes.
- Replace salt added to food during cooking with no-salt alternatives such as pepper, garlic, herbs, and spices.

Heart disease

Iron damage to the heart, leading to heart rhythm disturbances and weak pumping function, known as 'heart failure,' used to be leading causes of illness and early death for people with transfusion-dependent thalassaemia. Now, in most parts of the world, improved detection of iron in the heart, and its removal by intensive chelator treatment, has greatly improved this problem. However, heart and circulatory complications remain an issue.

- 'Atherosclerosis' describes thickening or hardening of the arteries, and several complications of thalassaemia can contribute to this, including inflammation in the vessels due to high circulating iron levels, diabetes and other hormone disturbances, and high blood pressure. We usually think of lipids like cholesterol increasing the risk of heart disease; in people with thalassaemia cholesterol levels are often low, but unfortunately the level of the 'good', heart-protective type of cholesterol called high-density lipid or HDL is frequently low too.
- Low levels of vitamin D, and the trace elements zinc and selenium, have been associated with heart disease in the general population, and measurement and correction of these may help.
- Dietary intake of saturated and trans fats – mainly found in fats of animal origin but also in palm and coconut oil, and in fried or battered foods - should be limited, and some popular but possibly harmful diets such as ketogenic and liquid protein diets, the Southern and other diets should be avoided altogether! Energy drinks and alcohol should be taken in limited amounts if at all, and it goes without saying, smoking should absolutely be avoided.
- By contrast, other nutrients can have heart-protective properties. These include fish, nuts, and other foods rich in omega-3 polyunsaturated fatty acids, such as are prevalent in the Mediterranean diet; a good intake of these is therefore encouraged.

Kidney stones

These are quite common in the general population, but in adults with thalassaemia are about twice as common and can affect up to 1 in 2 people. They are mainly composed of calcium salts. They sometimes do not cause symptoms, but can cause repeated urine infections, bleeding into the urine, or – if small stones pass from the kidney down the tube into the bladder – may cause very severe pain spasms called 'renal colic'. They can also contribute to long-term kidney malfunction.

The causes for the increased rates of stone formation aren't entirely clear, but probably relate in part to increased concentrations of calcium in the urine, which can be associated with underactive parathyroid gland, diabetes, and high bone turnover. Iron chelation may also contribute – but of course can't be avoided if iron levels are to be kept in the safe range. Kidney stones are more common in people who are overweight, or very sedentary, and whose sodium intake is high. Insufficient fluid intake makes the urine more concentrated and can worsen the problem.

The following guidance applies to people in general who tend to form kidney stones, and can be applied to people with thalassaemia also:

- Encourage adequate hydration >2.5 L/day.
- Limit sodium intake to under 5 g / day – no more than a level teaspoon.
- Encourage 5 to 7 portions of fruits and/or vegetables per day.
- Maintain body mass index (BMI) to between 18 – 24 kg/m2.
- Participate in regular physical activity.
- Consume calcium from the diet as opposed to supplementation.
- Keep vitamin D levels between 30 – 50 ng/mL.
- If diabetic, manage blood glucose levels.
- Consume no more than 1000 mg of vitamin C per day.

7. Recommendations

The recommendations and advice provided here are based on both the scientific research as well as clinical experience of clinicians who regularly take care of people with thalassaemia. Before making any significant changes to your diet, medications, or exercise habits, it is always best to discuss them with your doctor, nutrition specialist or specialist nurse.

- Consume a varied nutrient-dense diet, with fruits and vegetables every day.
- Hydrate frequently, drinking mostly water and non-sugar sweetened beverages.
- Include foods rich in whole grains in your diet.
- Take a vitamin D supplement (either vitamin D2 (ergocalciferol) or D3 (cholecalciferol) at a dose of 1,000 – 2,000 IU/day or 50,000 IU monthly and have vitamin D levels checked at least annually.
- Assess vitamin C annually as it may be useful for optimal chelator medication function. If deficiency is observed, care should be taken to ensure adequate chelation while supplementing with vitamin C.
- Consume a diet rich in foods with high Vitamin E content, such as wheat germ, nuts, and vegetable oils (olive, canola, sunflower, avocado)
- Include foods rich in folate (e.g. dark green leafy vegetables, whole grains, beans)
- Assess zinc annually. If deficient, supplement with 25 mg zinc/day preferably as zinc gluconate, acetate, or citrate.
- Restrict dietary iron intake only if a non-transfusion dependent patient. Iron restriction should not be a primary focus for transfusion dependent patients where the amount of iron from transfusion far outweighs dietary iron absorption.
- Drinking tea with meals may be of benefit for patients with non-transfusion dependent thalassaemia to reduce iron absorption.
- Botanicals such as turmeric, wheatgrass and silymarin may have some benefits in reducing iron toxicity and protecting the liver. Talk with your doctor before starting on any new supplement.
- Consider taking a multi-vitamin mineral supplement without iron, though supplementation of any kind should not take the place of a varied diet that is rich in fruits and vegetables.

Avoid/Limit:

- Limit intake of foods with added sugars
- Avoid smoking cigarettes.
- If you are on a blood thinning or 'anticoagulant' medication and vitamin K supplementation is recommended, it should be taken regularly; inconsistency can make some anticoagulants less effective.
- Limit alcohol consumption. People with any evidence of liver inflammation – from iron build-up, or viral hepatitis infection, or any other cause – should avoid it altogether. Others should drink alcohol only in moderation, not exceeding two drinks a day for men and one for women, and with some alcohol-free days each week.

Physical Activity

- Participate in non-contact, weight bearing activity (e.g. walking regimes) every day after consultation with your haematologist and/or cardiologist.
- Consider adding activities that promote flexibility and enhance core strength and balance such as yoga or Pilates.
- Nutrition and physical activity cannot, of course, take the place of other medical advice but all the approaches can work together to enhance health and wellbeing.

Glossary

Antioxidant: a substance that protects the body from free radicals and oxidative stress] [see below]. Examples of antioxidant nutrients include Vitamin C, E, selenium, and zinc.

Body Mass Index (BMI): calculated by dividing body weight in kg by height in meters squared. A simple indicator of under (<18 kg/m2) or overweight (>25 kg/m2).

Complete Protein: A dietary protein that contains all 8 essential amino acids. All animal protein is complete (e.g. beef, poultry, fish, eggs, dairy), while most vegetable protein is incomplete (e.g. beans, nuts).

Chelator: type of medication which removes iron from the body. There are 3 types of chelator medications, 2 are taken by mouth (deferasirox, deferiprone), the other (deferoxamine or desferrioxamine) is given through a needle and infused under the skin over several hours at a time.

Diabetes mellitus: a condition in which your body cannot handle dietary sugars which leads to elevated circulating blood glucose.

Enzymes: proteins our body cells make which help speed up metabolism, or the chemical reactions in our bodies.

HDL: high density lipoprotein, the 'good' fat, higher circulating levels of HDLs are associated with reduced cardiovascular risk.

LDL: low density lipoprotein, the 'bad' fat, higher circulating levels of LDLs are associated with cardiovascular risk.

Magnesium: an essential mineral, found in whole grains, dark green leafy vegetables, legumes and nuts, important for bone health.

Nutrient density: the amount of nutritional value per calorie. Foods with poor nutrient density have few nutrients per calorie, or often referred to as 'empty calorie' foods, as they provide energy but little else.

Nephrolithiasis: another term for kidney stones.

Osteoporosis: a condition of thin or weak bones which are more likely to fracture.

Oxidative stress:

- **Free Radicals:** In the process of metabolism, which is the total of the biochemical reactions in the body aiming to produce energy and maintain health in the various tissues and organs, one by-product is the production of oxygen-containing molecules, which are called free radicals. These free radicals can react with other molecules in a process called oxidation, with other by-products which can be harmful. For this reason, there is another set of molecules which can make the free radicals less reactive and so less harmful; these are called antioxidants.
- **Oxidative Stress:** So, in normal situation there is a balance between free radicals (oxidants) and antioxidants. If this balance is disturbed, and harmful oxidants are in excess, then this is called oxidative stress.

Saturated fats: type of dietary fat frequently found in animal products and butter, these types of fats are typically solid at room temperature.

Unsaturated fats: type of dietary fat frequently found in vegetable oils (e.g. olive, canola, sunflower), avocados, seeds, nuts and nut butters (peanut butter). These dietary fats are typically liquid at room temperature.

Trans Fats: type of dietary fat frequently found in fried and processed foods (cookies, crackers, cakes) and is associated with increased cholesterol levels and cardiovascular risk.

Vitamin K: an essential vitamin found in dark green leafy vegetables and some fermented foods, important for blood clotting, bone health, vitamin D function.

Further Reading

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ABOUT THE THALASSAEMIA INTERNATIONAL FEDERATION (TIF)

Thalassaemia International Federation (TIF), a non-governmental, patient driven umbrella organisation, established in 1986, supports today, the rights of patients for access to quality health, social and other care through its work with over 200 national thalassaemia associations in 62 countries across the world. It was founded by a small group of doctors and patients/parents who represented National Patient Associations, mainly from Cyprus, Greece, Italy, UK and USA i.e. Countries where thalassaemia had been recognized early as a genetic, hereditary disorder with huge medical, public, health, social and economic repercussions if left unaddressed in terms of both effective prevention and management. Thus, these were the countries where strong research activity was initiated and the first control programmes were implemented in the early 1980s, with measurable success. The rationale of these founding members lay on the establishment of an international umbrella organization to build on the accumulated experience and the knowledge gained, aiming to support the efforts of the other countries since in the mid-1980s the worldwide prevalence of the disease had been well verified.

Our Mission: The prioritisation of thalassaemia on national health agendas and the development and implementation of effective disease-specific control (prevention and clinical management) programmes within national healthcare systems based on universal coverage

Our Vision: To support the provision of equal access of every patient with thalassaemia to high quality health, social and other care in a truly patient-centred healthcare setting

Our Values: Transparency, reliability, ethos, accountability, independence and patient-centredness

Our Work:
- Education • Advocacy • Collaborations/ Networking
- Research • Raising Awareness

Our Partners:
- World Health Organisation:
- United Nations: in special consultative status with the United Nations Economic and Social Council (ECOSOC) since 2017
- Council of Europe: participatory status in the Conference of International NGOs since 2019
- European Union:

Our Motto: Unity & Knowledge Constitute our Strength!

THALIA

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