TUTORIAL 3

MICRONUTRIENTS

OVERAL OBJECTIVES

At the end of this module the student should be able to:

a) Take a dietary history and growth history of children
b) Describe the signs and symptoms of micronutrient deficiency
c) Recognise by appropriate examination, common and life threatening complications of micronutrient deficiencies in infants and children and investigate and manage these complications.

Signs & symptoms of micronutrient deficiency

The specific examination of child, who grows poorly, needs full clinical examination focusing on the cause, degree and complications of malnutrition. It is therefore important, to learn the signs and symptoms of deficiency of individual vitamins, minerals and trace elements.

Classification of micronutrients

1. Vitamins
    a. Fat soluble vitamins
    b. Water soluble vitamins
2. Minerals
3. Trace elements

1. VITAMINS

Vitamins are organic dietary constituents necessary for life, health, and growth that do not function by supplying energy. These are the substances that act as co-enzymes and are regulators of metabolic processes.

a. Fat soluble vitamins

i. Vitamin A: Retinol

It is constituent of visual pigments, necessary for foetal development and for cell development throughout the life.

Signs of deficiency

- Night blindness
- Xerophthalmia – dry eyes due to inadequate production of tears
- Conjuctival xerosis – dryness of eye membrane
- Corneal xerosis – dryness of cornea
- Keratomelacia – softening of cornea – seen in infancy
- Bitots spots in school children
- Follicular hyperkeratosis of skin

Signs of hypervitaminosis

- Irritabilty & anorexia
- Headache and bone pain

- Hepatosplenomegaly
- Scaly dermatitis & patchy loss of hair

ii. Vitamin D: Cholecalciferol

It increases intestinal absorption of calcium and phosphate and promotes normal bone formation and mineralization

Signs of deficiency

- Rickets:
    - Epiphyseal enlargement – painless – over 6 months of age
    - Beading of ribs – rachitic rosary
    - Bowed legs and knocked knees
- Persistanty open anterior fontanelle after 18 months
- Frontal bossing
- Craniotabes < 1 yr
- Delayed dentician/poor dentition
- Rachitic tetany caused by hypocalcaemia

Signs of hypervitaminosis

- Weight loss
- Calcification of many soft tissues, and eventual renal failure

iii. Vitamin E: Tocopherol

- Cholestasis and Cystic fibrosis are important causes of deficiency
- Clinical deficiency does not appear until 1 year of age, even in children with cholestasis since birth
- It functions as an anti-oxidant; precise biochemical functions unknown
- It is also a co-factor in electron transport in cytochrome chain

Signs of deficiency

- Loss of deep tendon reflexes
- Limb ataxia, intention tremor, dysdiadochokinesia
- Truncal ataxia: wide based unsteady gait
- Ophthalmoplegia: limitation of upward gaze
- Nystagmus
- Decreased proprioception: positive Romberg test
- Visual field constriction: may progress to blindness
- In premature infants: haemolysis of RBCs during 2nd month of life
- Haemolytic anaemia in preterm infants: oedema may also be present
- Young children with congenital cholestasis: a genetically inherited rare disease – familial isolated vitamin E (FIVE) deficiency. Despite normal lipid absorption they have low undetactable level of plasma vitamin E. Reduced tendon reflexes occur at 3-4 yrs of age and disabling cerebrospinal symptoms occur by early adolescence.

iv. Vitamin K: Phytomenadion

It catalyzes gama carboxylation of glutamic acid residues on various proteins concerned with blood clotting. It is essential for production of coagulation factors: 2, 7, 9 , 10 and other factors like protein C, S, Z

Signs of deficiency

- Easy bruisability: look for patechiae and bruising
- Conjunctival haemorrhages
- Mocosal bleeding
- GIT haemorrhage, haematuria and epistaxis

Signs of hypervitaminosis

- Gastrointestinal disturbances
- Anaemia

b. Water soluble vitamins

i. Vitamin B1: Thiamine

It is cofactor for decarboxylations.

Signs of deficiency

Beriberi & neuritis

- **Dry beriberi**
  - Pain - tingling or loss of sensation in hands and feet – peripheral neuropathy
  - Muscle wasting – loss of function and paralysis of lower extremities
- **Wet beriberi**
  - Oedema - lung congestion
  - Cardiomegaly – Congestive cardiac failure (CCF)
- **Infantile beriberi**
  - Convulsions and acute cardiac failure in early months of life

ii. Vitamin B2: Riboflavin

It is constituent of flavoprotein enzymes which are important in oxidation reduction reactions.

- It act as co-enzyme in carbohydtrate metabolism
- It is also needed to process fats and amino acids
- It activates vitamin B6 and folic acid

Signs of deficiency

- Cataracts – corneal vascularization – blurred vision
- Burning and itching of eyes
- Reddening of lips – cheilosis
- Glossitis – magenta tongue
- Delayed mental response

iii. Vitamin B3: Niacine

It is the constituent of NAD & NADP: coenzymes in numerous oxidative reduction reactions.

Signs of deficiency

- Pallegra
- 3D: diarrhoea, dementia, dermatitis
- Tongue fissuring
- Malar and supraorbital pigmentation
- Hyperpigmented skin rash in sun exposed areas

iv. Vitamin B5: Pantothenic acid

It is an important component of co-enzyme A and Acyle carrier protein involved in fatty acid metabolism.

Signs of deficiency

- Dermatitis
- Alopecia
- Numbness
- Paresthesias
- Muscle cramps
- Adrenal insuffficiency

v. Vitamin B6: pyridoxine

It forms prosthetic group of certain decarboxylases and transaminases and gets converted in body into pyridoxal phosphate & pyridoxamine phosphate. It is also constituent of co-enzymes for fatty acid metabolism, haem synthesis and is essential for homocystein metabolism.

Signs of deficiency

- Peripheral neuritis in patients receiving INH
- Convulsions in infants
- Hyperirritability
- Hypochromic anaemia

vi. Vitamin B9: Folic acid

- It is important for synthesis of DNA, RNA and nuclear proteins
- It is used in the metabolism of homocysteine so its deficiency leads to accumulation of homocystein in the body

Signs of deficiency

- Sprue
- Pale conjunctiva: megaloblastic anaemia
- Congenital abnormalities in the new born: spina bifida
- Coronary artery disease and stroke: due to accumulation of homocysteine

vii. Vitamin B12: Cyanocobalamine

It act as coenzyme in amino acid metabolism & stimulates erythropoiesis. It plays an important role in DNA synthesis and neurological function.

Signs of deficiency

- Pale conjunctiva: megaloblastic anaemia
- Loss of appetite intermittent diarrhoea or constipation
- Numbness and tingling sensation in hands
- Optic neuritis: optic nerve inflammation
- Romberg's sign
- Jaundice

B1, B6, B12 deficiency: main features: peripheral neuropathy and decreased knee & ankle jerks

viii. Biotin

It catalyzes carbon dioxide "fixation" (in fatty acid synthesis).

Signs of deficiency

- Dermatitis
- Enteritis
- Seborrhoea
- Alopecia
- Conjunctivitis

ix. Vitamin C: Ascorbic acid

- It maintains prosthetic metal ions in their reduced form and scavenges free radicals.
- It protect folic acid reductase, which converts folic acid to folinic acid
- It maintains non-haem Fe absorption and Fe transfer from transferrin to ferritin

Signs of deficiency

- Scurvy: haemorrhagic manifestations and abnormal bone and dentine formation
- Spongy and bleeding gums, infection, gangrene, losening of teeth at later stage
- Slow healing of wounds
- Bowing of long bones epiphyseal enlargement (painful)
- Haemorrhages under the skin intramuscular and subperiosteal haematoma
- Follicular hyperkeratosis

Infentile scurvy

- Haematoma formation
- Painful epiphyseal enlargement especially at costochondral junction
- Spongy bleeding gums: does not occure in the absence of teeth

2. MINERALS

i. Calcium

- It has important role in cell permeability, bone and teeth formation
- It is essential for blood co-agulation, transmission of nerve impulses and normal muscle contraction

Signs of deficiency

- Irritability – reptitive muscle spasms
- Twitching corpopedal spasm tetany
- Cardiac arrythemias
- Chvostek's sign / Troussea's sign
- Decreased muscle tone – weakness – lethargy

ii. Phosphorous

- It forms structure of teeth, bones and cell membrane
- It is an important component of ATP and forms RNA and DNA
- Deficiency of Phosphate can cause reduction of 2,3 DPG levels in RBCs which decreases the oxygen delivery to tissues. It can also cause Haemolysis & dysfunction of white blood cells

Signs of deficiency

- Rickets
- Delayed dentition and tooth abscesses
- Short stature without clinical evidence of bone disease
- Rhabdomyolysis
- Proximal muscle weakness and atrophy
- Cardiomegally / cardiac failure

iii. Magnesium

Hypomagnesaemia causes secondary hypocalcaemia by imparing release of PTH by parathyroid gland and through blunting the tissue response to PTH.

Signs of deficiency

- Tetany
- Positive Chvostek and Trousseu signs
- Seizures

iv. Sodium

Most of the body sodium is located in blood and in the fluid round cells. It helps the body keep fluids in a normal balance, plays a key role in normal nerve and muscle function.

Signs of deficiency

Brain cell swelling is responsible for most symptoms

- Anorexia, nausea and vomiting

- Confusion and lethargy
- Headach, seizures and coma and decreased reflexes
- Cheyn Stokes respiration
- Muscle cramps and weakness
- Chronic hyponatraemia may be asymptomatic: owing to a compensatory decrease in brain cell osmolality which limits brain swelling

v. Potassium

It helps regulate fluid balance, muscle contractions and nerve signals.

Signs of deficiency

- Ventricular fibrillation
- Skeletal muscle weakness and cramps
- Paralysis: if potassium < 2.5 – starts with legs followed by arms
- Respiratory paralysis: some may develop rhabdomyolysis
- Constipation: ilius, due to slow GIT motility
- May cause polyuria by producing secondary nephrogenic diabetes insipidus

3. TRACE ELEMENTS

By definition a trace element is the one which is required in <0.01% of the body weight to maintain normal body growth

i. Copper

It is the component of enzymes involved in:

- Energy production through cytochrome oxidase
- Protection of cells from free redical damage through supperoxide dismutase
- Brain neurotransmitters through dopamine hydroxylase
- Also involved in absorption, storage and metabolism of iron

Signs of deficiency

- Microcytic anaemia
- Neutropenia
- Osteoporosis
- Depigmentation of hair and skin

ii. Iron

It is the main component of haemoglobin and myoglobin.

Signs of deficiency

- Pale conjunctiva: Fe deficiency anaemia
- Kiolonychia: spoon shaped nails – in older children and adults
- Toungue – atrophic lingula papillae
- Angular stomatitis
- Decreased alertness

- Impaired learning

iii. Zinc

It is essential for body's immune system. It plays a role in cell devision, cell growth, wound healing and breakdown of carbohydrates. Its supplementation is beneficial in diarrhoea and to improve neurodevelopmental outcome.

Signs of deficiency

- Hypogonadism: delayed puberty
- Skin changes: particularly associated with a rash – dermititis of extremities and around orifices
- Impaired immunity, poor wound healing
- Diarrhoea
- Mental lethargy

iv. Manganese

It is an enzyme co-factor. It is essential for connective tissue, bones, clotting factors and sex hormones. It is also necessary for normal brain & nerve function and blood sugar regulation.

Signs of deficiency

- Hypercholesterolaemia
- Decreased clotting proteins
- Memory disturbance
- Tiredness: mysthenia gravis
- Ataxia: fainting
- Hearing loss

v. Iodine

Component of thyroid hormone

Signs of deficiency

- Goiter
- Coarse facies, dry skin
- Lethargy
- Jaundice
- Large tongue
- Bradycardia
- Wide posterior fontanelle
- Hypothermia
- Constipation

vi. Fluroide

It is the main constituent of bone and forms an active componenet of teeth enamel.

Signs of deficiency

- Brittle bones
- Dental caries

[enamel defects (vit D), looseness (vit C)]

vii. Selenium

It plays a role in metabolism & thyroid function and prevents oxidative damage

Signs of deficiency

- Myopathy
- Fatigue
- Hyperthyroidism
- Lack of mental dexterity
- Keshan disease: it is congestive cardiomyopathy (myocardial necrosis which leads to weakneing of the heart muscle) caused by a combination of dietary deficiency of selenium and the presence of a mutated strain of Coxsackievirus.

EXAMINATION OF A CHILD FOR MICRONUTRIENT DEFICIENCY

After full anthropometric assessment child need to be assessed for specific deficiencies of micronutrients including vitamins, minerals and trace elements. Expose the child from head to toe. Put up the nappy or undergarments after examining the genitalia and perineum. Avoid undue and long exposure.

Following clinical signs may be noted in micronutrient deficiency

Hair changes	Reddish brown, brittle and sparse hair	Sever acute malnutrition
	Depigmentation of hair and skin (Kinky hair)	Copper deficiency
Skull	Microcephaly	Chronic malnutrition
	Bossing of skull Craniotabes Delayed closure of fontanels	Vitamin D deficiency
Eye changes	Night blindness Xerophthalmia Xerosis conjunctivae Xerosis cornia Keratomalacia Corneal perforation	Vitamin A deficiency
Mucous membranes lesiosns	Angular stomatitis Atrophic glossitis	Fe deficiency
	Reddish cracks in lips (cheilosis)	Vitamin B2 defiency
	Swolen, spongy and bleeding gums	Vitamin C deficieny
	Patechiae Mocosal bleeding	Vitamin K deficiecny
Tongue	Smooth reddish tongue (Glossitis)	Severe acute malnutrition Vitamin B2 deficiency Pellagra
Teeth	Brittle bones and dental caries	Floride deficiency
Neck	Goiter Coarse facies Large tongue Bradycardia Wide posterior fontanelle or delay in closure of fontaneles	Iodine deficiency Hypothyroidism
Chest	Rickety-rosary Harrison sulcus Pectus carinatum or Pectus excavatum	Vitamin D deficiency Phosphate deficiency

Skeletal abnormalities	Broadening of wrists & ankles Kyphosis, scoliosis or lordosis Legs: X or O or laterlised deformaity Tetanic spams	Vitamin D deficiency Phosphate deficiency
	Loss of deep tendon reflexes Limb ataxia Truncal ataxia	Vitamin E deficiency
	Peripheral neuropathy and decreased knee & ankle jerks Numbness and tingling sensation of hands	Vit B1, B6 and B12 Deficiency
	Abnormal bone and dentine formation Pseudoparalysis Tender epiphyseal enlargement	Vitamin C deficieny
	Twitching & corpopedal spasm (tetany) Chvostek's sign Troussea's sign	Calcium and or magnisium deficiency
	Skeletal muscle weakness and muscle cramps	Potassium deficiency
Skin	Follicular hyperkeratosis (shouldrs, gluteal area and extensor surfaces of extremities	Vitamin A deficiency
	Hyperpigmentation of sun exposed parts	Nicotinic acid deficiency: Pellegra
	Depigmentation or hyperpigmentation of flanks with wet and raw lesions in diaper area	Sever acute malnutrition
	Easy bruisability Patechiae and bruising Conjunctival haemorrhages Mocosal bleeding	Vitamin K deficiecny
	Poor wound healing Hypogonadism Delayed puberty Impaired immunity Mental lethargy	Zinc deficiency
Palmer pallor	Pale palms Pale conjunctivae	Fe, folate or B12 deficiency anaemia
Nails	Brittleness of nails Kiolonychia: spoon shaped nails (in older children and adults)	Fe deficiency

Organomegaly	Hepatomegaly	Severe acute malnutrition
	History of pica & Spleenomegaly	Fe deficiency
Non specific symptoms	Irratability Loss of appetite Easy fatiguability Decreased alertness Impaired learning	Fe deficiency Vitamin D deficiency Vitamin C deficiency Sever acute malnutrition

Lastley make summary of your assessment and exclude Refeeding Syndrome (RFS) in the child if he is already receiving treatment.

Refeeding Syndrome (RFS)

- There is no agreed international definition of RFS.
- It is a syndrome of severe electrolyte and fluid shifts associated with metabolic abnormalities in malnourished patients undergoing refeeding, whether orally, enterally, or parenterally
- Hypophosphataemia is the adopted surrogate marker for diagnosing RFS though low phosphate is not pathognomic as hypophosphataemia is uncommon in hospitalised patient population
- Symptoms occur because changes in serum electrolytes affect the cell membrane potential impairing the function in nerve, cardiac and skeletal cells
- Spectrum of symptoms ranges from simple nausea, vomiting, and lethargy to respiratory insufficiency, cardiac failure, hypotension, arrythmias, delirium, coma and death
- Prevention is the key to successful management: early identification of high risk individuals, monitoring during refeeding, and an appropriate feeding regimen
- Principles of management are to correct biochemical abnormalities and fluid imbalances returning levels to normal where possible