CHAPTER- I

INTRODUCTION
The process by which substances in food are transformed into body tissues and provide energy for physical and mental activities that makes up human life is called as human nutrition. The major issues of human nutrition are energy generation and balance, requirement of essential nutrients. The study of human nutrition is interdisciplinary involving not only physiology, biochemistry and molecular biology but also psychology and anthropology. This further touches on economics and political science as the world recognizes and responds to the suffering and death caused by malnutrition. The ultimate goal of nutritional science is to promote optimal health and to reduce the risk of chronic diseases. Dietary guidelines will be prescribed in order to provide good health and uplift living standards.

Nutrients can be classified broadly into two groups namely macro and micro nutrients. Macronutrients constitute three classes - carbohydrates, lipids (fats and oils) and proteins which provide raw materials for tissue building and maintenance as well as fuel to run the myriad of physiological and metabolic activities that sustain life. In contrast, three classes of micronutrients which are not energy sources but facilitate metabolic processes throughout the body are vitamins, minerals and water. Depending upon the essentiality of vitamins in human body, it is proposed to understand their status in various populations.

Vitamins are organic compounds found in living organisms in very small amounts for supporting cellular activities[^1]. The name vitamin is obtained from "vital amines" as it was originally thought that these substances were all amines. These compounds are essential for the growth and development of the body and in turn support life functions. Even from the moment of conception onwards, the fetus inside the mother absorbs these nutrients. Even though humans are able to synthesize certain vitamins to some extent, they depend upon diet for their supplementation.

When it is in short supply or is not able to be utilized properly, then it causes a specific deficiency syndrome. When deficient vitamin is supplied before irreversible damage occurs, the signs and symptoms are reversed. The amount of vitamins required on daily basis is recommended in milligrams or micrograms.
Discovery of vitamins with their chemical names, dietary allowances and deficiency diseases are furnished in Table 01.

Table 01: Vitamins with their chemical name, year of discovery and deficiency diseases:[P-R/1227]:

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Year of Discovery</th>
<th>Recommended dietary allowances</th>
<th>Deficiency diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (Retinol)</td>
<td>1909</td>
<td>900 µg</td>
<td>Night blindness and Keratomalacia</td>
</tr>
<tr>
<td>Vitamin D (Calciferol)</td>
<td>1918</td>
<td>5 – 10 µg</td>
<td>Rickets and Osteomalacia</td>
</tr>
<tr>
<td>Vitamin E (Tocopherol)</td>
<td>1922</td>
<td>15 mg</td>
<td>It is very rare; mild hemolytic anemia in newborn infants.</td>
</tr>
<tr>
<td>Vitamin K (Phylloquinone)</td>
<td>1929</td>
<td>120 µg</td>
<td>Bleeding diathesis</td>
</tr>
<tr>
<td>Vitamin C (Ascorbic acid)</td>
<td>1912</td>
<td>90 mg</td>
<td>Scurvy</td>
</tr>
<tr>
<td>Vitamin B₁ (Thamine)</td>
<td>1912</td>
<td>1.2 mg</td>
<td>Beriberi, Wernicke-Korsakoff syndrome</td>
</tr>
<tr>
<td>Vitamin B₂ (Riboflavin)</td>
<td>1920</td>
<td>1.3 mg</td>
<td>Aripoflaviniosis</td>
</tr>
<tr>
<td>Vitamin B₃ (Niacin)</td>
<td>1936</td>
<td>16 mg</td>
<td>Pellagra</td>
</tr>
<tr>
<td>Vitamin B₅ (Pantothenic acid)</td>
<td>1931</td>
<td>5 mg</td>
<td>Paresthesia</td>
</tr>
<tr>
<td>Vitamin B₆ (Pyridoxine)</td>
<td>1934</td>
<td>1.3 - 1.7 mg</td>
<td>Anemia</td>
</tr>
<tr>
<td>Vitamin B₇ (Biotin)</td>
<td>1931</td>
<td>30 µg</td>
<td>Dermatitis and Enteritis</td>
</tr>
<tr>
<td>Vitamin B₉ (Folic acid)</td>
<td>1941</td>
<td>400 µg</td>
<td>During pregnancy is associated with birth defects, like neural tube defects</td>
</tr>
<tr>
<td>Vitamin B₁₂ (Cyanocobalamin)</td>
<td>1926</td>
<td>2.4 µg</td>
<td>Megaloblastic anemia</td>
</tr>
</tbody>
</table>

Vitamins were also artificially synthesized. B-complex vitamins are synthesized by the microorganisms in the intestinal tract. They can be stored in the body to some extent, like fat-soluble vitamins stored in the liver and subcutaneous tissue. The total daily requirement for humans is usually very small.

**Importance of vitamins:**

* Vitamin A is essential for growth and body repair. It is vital in the formation of bone, tissues and also keeps skin smooth. Its deficiency causes night blindness.

* Vitamin D is important for bone development and sustenance whose deficiency causes rickets in children and osteoporosis in adults.

* Vitamin E is essential to prevent sterility and cell damage due to aging, to break up blood clots and for wound treatment.
* Vitamin K is involved in carboxylation of certain glutamate residues in proteins to form γ-carboxyglutamate residues (Gla-residues) which plays key role in regulation of blood coagulation, bone metabolism and vascular biology.

* Vitamin C is essential for synthesis of collagen and for protection of bones, teeth and gums. It is an ultimate medicine for scurvy and body resistance.

* Vitamin B₃ is an energy building vitamin which helps to digest carbohydrates. It also keeps heart and muscles stable.

* Vitamin B₂ along with B₉ helps in the formation of red blood cells (R.B.C).

* Vitamin B₃ is required for proper functioning of more than 50 enzymes and helps to release energy or make fats from carbohydrates. It is also used to make sex hormones and other important chemical signal molecules.

* Vitamin B₅ is needed to form coenzyme-A (CoA) and its role is critical in the metabolism and synthesis of carbohydrates, proteins and fats.

* Vitamin B₆ is necessary for metabolism of proteins and production of antibodies.

* Vitamin B₇ promotes the health of sweat glands, nerve tissue, bone marrow, male sex glands, blood cells, skin and hair.

* Vitamin B₉ protects against birth defects by helping regulate embryonic and fetal nerve cell formation. This reduces the risk of heart attack by lowering homocysteine levels. It strengthens the immune system by aiding the proper formation and functioning of white blood cells(W.B.C)

* Vitamin B₁₂ is required for the metabolism of carbohydrate and lipids which is a must for children’s growth.

**Role of vitamins in disease:** Deficiencies of vitamins causes disease condition due to malnutrition or malabsorption. A serious deficiency in one or more of these vitamins may develop a deficiency disease. Even minor deficiencies may cause permanent damage. Deficiency of vitamins is classified as either primary or secondary.

**Primary Deficiency:** It may develop due to lack of vitamins in the diet.
**Secondary Deficiency:** This may be due to an underlying disorder that prevents or limits the absorption or use of the vitamin, due to a “lifestyle factor”, such as smoking, excessive consumption of alcohol or the use of medications that interfere with the absorption or use of the vitamin.

**Types of Vitamins:** The 13 vitamins known to be required by human body are categorized into two groups according to their solubility. The four fat soluble vitamins (soluble in nonpolar solvents) are vitamins A, D, E and K. The nine water soluble vitamins (soluble in polar solvents) are vitamin C and the eight B-complex vitamins: B\(_1\) (Thiamin), B\(_2\) (Riboflavin), B\(_3\) (Nicotinic acid), B\(_4\) (Nicotinamide), B\(_5\) (Pantothenic acid), B\(_6\) (Pyridoxine), B\(_7\) (Biotin), B\(_9\) (Folic acid) and B\(_12\) (Cyanocobalamin). The following vitamins are being dealt in the present investigation.

**Fat-soluble:** The 4 fat-soluble vitamins are A, D, E and K which have different chemical forms, from these a single form of vitamin was investigated in this study. These are absorbed through the intestinal tract with the help of lipids (fats). Their accumulation in the body leads to hypervitaminosis. Absorption of fat-soluble vitamins requires the presence of bile acids/salts. Once these vitamins are absorbed, the body stores them in body fat. Consumption of saturated and unsaturated fats or oils may cause shortage of fat-soluble vitamins. They should not be consumed in excess since it may result in causing side effects.

**Vitamin A (Retinol):** The animal form of vitamin A is important in vision and bone growth. It is a diterpenoid. Retinol is one among the most useable forms of vitamin A. Molecular formula of retinol is C\(_{20}\)H\(_{30}\)O. Many different geometric isomers of retinol, retinal and retinoic acid are possible as a result of either a trans or cis configuration of 4 of the 5 double bonds found in the polynene chain. The cis isomers are less stable and can be readily converted to all-trans configuration.

**Forms:** Three forms of vitamin A include: Retinal (aldehyde form), Retinoic acid (acid form) and Retinyl ester (ester form). These chemical compounds are collectively known as retinoids and all possess the biological activity of all-trans retinol as a common feature in their structure. Structurally, retinoids possess a β-ionone ring and a polyunsaturated side chain, with an
alcohol, aldehyde, a carboxylic acid group or an ester group. The side chain is composed of 4 isoprenoid units, with a series of conjugated double bonds which may exist in trans or cis configuration. The structure of retinol is shown in Figure 01.

**Functions:** Retinoic acid via the retinoic acid receptor influences the process of cell differentiation, growth and development of embryos. It is used in differentiation of stem cells as well.

Retinoic acid regulates gene expression by activating intracellular retinoic acid receptors. These functions are essential in the immunological, reproductive and embryonic development of vertebrates as evidenced by the impaired growth, susceptibility to infection and birth defects observed in populations receiving suboptimal vitamin A in their diet.

Vitamin A is required in the production of rhodopsin, the visual pigment used in low light levels. It is essential for the correct functioning of epithelial cells and to maintain intact epithelial tissues as a physical barrier to infection. Glycoprotein synthesis requires adequate levels of vitamin A. It is needed for normal haematopoiesis and its deficiency causes abnormalities in iron metabolism. The vitamin affects the production of human growth hormone. It also plays an essential role in vision, particularly night vision, normal bone and tooth development, reproduction and the health of skin and mucous membranes. It also acts an antioxidant, a protective chemical that may reduce the risk of certain cancers.

**Sources:** Dietary sources of vitamin A are retinoids and carotenoids. The former consists of retinal and retinol. Provitamin retinol is converted to active form by the body. Carotenoids, well known as B-carotene also form of retinol. Animal sources (liver, eggs and fortified dairy products) contain retinyl esters whereas plants, leafy vegetables and darkly colored fruits (carrots, spinach) contain pro-vitamin A carotenoids.

**Deficiency:** Night blindness is one of the first signs of vitamin A deficiency. Its deficiency also contributes to blindness by making the cornea very dry and damaging the retina and cornea.
**Vitamin D (Cholecalciferol):** This belongs to a group of fat-soluble prohormones and it has no hormonal activity by itself. It is converted to the active hormone 1, 25-dihydroxycholecalciferol through a tightly regulated synthetic mechanism. Its production in nature always requires the presence of some UV light; even in foodstuffs it is ultimately derived from organisms, from mushrooms to animals, which are not able to synthesize it except through the action of sunlight at some point in the synthetic chain. The term vitamin D also refers to metabolites and other analogues of these substances. Molecular formula of cholecalciferol is C_{24}H_{44}O and its IUPAC name is (3β, 5Z, 7E) - 9, 10-secocholesta-5,7,10(19)-trien-3-ol. The structure of D₃ is represented in the Figure 02.

**Forms:** The five forms of vitamin D are: Vitamin D₁ (ergocalciferol with lumisterol, 1:1), Vitamin D₂ (ergocalciferol made from ergosterol), Vitamin D₃ (cholecalciferol made from 7-dehydrocholestrol in the skin), Vitamin D₄ (dihydroergocalciferol) and Vitamin D₅ (sitocalciferol made from 7-dehydrositosterol) [P-R/B15]. Vitamin D₃ is produced in skin exposed to sunlight, specifically ultraviolet B (UVB) radiation. Vitamin D₃ is made in the skin when 7-dehydrocholesterol reacts with UVB light at wavelengths between 270-300 nm, with peak synthesis occurring between 295-297 nm [62, 85]. These wavelengths are present in sunlight when the UV index is greater than 3. Adequate amounts of vitamin D₃ can be made in the skin after only 10 to 15 minutes of sun exposure at least two times per week to the face, arms and hands or back without sunscreen. With longer exposure to UVB rays, equilibrium is achieved in the skin and the vitamin simply degrades as fast as it is generated.

**Functions:** It regulates calcium and phosphorus levels in blood by promoting their absorption from the intestines and re-absorption of calcium in the kidneys which enables normal mineralization of bone and prevents hypocalcemic tetany. It is also needed for bone growth and remodeling by osteoblasts and osteoclasts [26, 121].
In the absence of vitamin K or with drugs (blood thinners) that interfere with Vitamin K metabolism, it can promote soft tissue calcification\[^{97}\].

- It inhibits parathyroid hormone secretion from the parathyroid gland \[^{113, 114}\].
- It affects immune system by promoting phagocytosis, anti-tumor activity and immunomodulatory functions \[^{120}\].

**Sources:** Vitamin D is naturally produced by the human body when exposed to direct sunlight. Foods such as milk, yogurt, margarine, oil spreads, breakfast cereal, pastries and bread are fortified with vitamin D\(_2\) and/or vitamin D\(_3\), to minimize the risk of its deficiency \[^{86}\]. Fish liver oils, such as cod liver oil and fatty fish species such as salmon, herring, catfish, mackerel, sardines, tuna and eel, egg and beef liver are also rich sources of vitamin D.

**Deficiency:** Deficiency results in impaired bone mineralization and leads to bone softening diseases such as rickets (a childhood disease characterized by impeded growth and deformity of the long bones)\[^{102}\], Osteomalacia (a bone-thinning disorder that occurs exclusively in adults and is characterized by proximal muscle weakness and bone fragility) and osteoporosis (a condition characterized by reduced bone mineral density and increased bone fragility).

**Vitamin E (α-Tocopherol):** Tocopherol (TCP), a class of chemical compounds of which many have vitamin E activity, are a series of organic compounds consisting of various methylated phenols. Because the vitamin activity was first identified in 1936 from a dietary fertility factor in rats, it was given the name “tocopherol”.

Tocotrienols, related compounds may also have vitamin E activity. These derivatives with vitamin activity may be referred to as “vitamin E.” Molecular formula of tocopherol is C\(_{29}\)H\(_{50}\)O\(_2\). Its IUPAC name is \((2R)\)-2,5,7,8-Tetramethyl-2-\([(4R,8R)\]-\(4,8,12\)-trimethyltridecyl]\)-6-chromanol.

Tocopherols and tocotrienols are fat-soluble antioxidants but also seem to have many other functions in the body. The compound α-
tocopherol is a common form of tocopherol added to food products. The chemical structure of tocopherol is given in Figure 03.

**Forms:** Vitamin E exists in 8 different forms: 4 tocopherols (α, R, R & R-tocopherols) and 4 tocotrienols (4 D-isomers). All the forms are determined by the number of methyl groups on the chromanol ring. Each form has slightly different biological activity [17].

**Functions:** It is used in manufacturing of skin creams and lotions which helps in encouraging skin healing and reducing scarring after injuries such as burns. It may prevent coronary heart disease [109], by limiting the oxidation of LDL-cholesterol (“bad” cholesterol).

It is an antioxidant, helps to protect the damaging effects of free radicals which may contribute to the development of chronic diseases like cancer. This may also block the formation of nitrosamines which are carcinogens formed in the stomach from nitrites consumed in the diet. It also combines with other antioxidants for preventing onset and progression of age related macular degeneration.

**Sources:** The most abundant sources of vitamin E are vegetable oils such as palm, sunflower, corn, soybean, almond, hazel nut, walnut and olive. Peanuts, chest nut, coconut, pollard, asparagus, oats, sunflower seeds, sea buckthorn berries, kiwifruit and wheat germ are also good sources. Other sources are whole grains, fish, butter, goat’s milk, tomatoes, carrot, green leafy vegetables and fortified breakfast cereals [P-R/B4].

**Deficiency:** Vitamin E deficiency causes neurological problems due to poor nerve conduction which include neuromuscular problems such as spinocerebellar ataxia and myopathies [16]. Its deficiency can also cause anemia, due to oxidative damage to R.B.C.
**Vitamin K (Menaquinone):** Its molecular formula is \( C_{31}H_{40}O_2 \) and its IUPAC name is 2'-methyl-3'-(2Z, 6E, 10E)-3, 7, 11, 15-tetramethylhexadeca-2'-2, 6, 10, 14-tetraen-1-yl] napthoquinone. It denotes a group of lipophilic, hydrophobic vitamins that are needed for the post translational modifications of certain proteins, mostly required for blood coagulation. The chemical structure of menaquinone is shown in the Figure 04.

**Forms:** Two natural and three synthetic forms are: Vitamin K\(_1\) (phylloquinone), vitamin K\(_2\) (menaquinone) and vitamin K\(_3\), K\(_4\) and K\(_5\) are synthetic forms.[P-R/B42].

**Functions:** It involves in the carboxylation of certain glutamate residues in proteins to form γ-carboxyglutamate residues (abbreviated Gla-residues). Gla-residues are usually involved in binding calcium which promotes osteotrophic processes and slows osteoclastic processes\[^{108}\]. The Gla-residues are essential for the biological activity of all known Gla-proteins\[^{39}\]. Fourteen human proteins with Gla domains (Gla-residues situated with specific protein domains) have been discovered and they play key roles in the regulation of three physiological processes:

- Blood coagulation: (prothrombin (factor II), factors VII, IX, X, protein C, protein S and protein Z) \[^{70}\].
- Bone metabolism: Osteocalcin also called as bone Gla-protein (BGP) and matrix Gla protein (MGP) \[^{98}\].
- Vascular biology\[^{14}\].

Vitamin K is used in treatment of Alzheimer’s disease\[^{4}\]. Vitamin K\(_2\) plays an important role in prevention of bone loss in females with liver diseases.

**Sources:** It is found chiefly in leafy green vegetables such as spinach, swiss chard and brassica (e.g. cabbage, kale, cauliflower, broccoli & brussels sprouts); some fruits such as avocado and kiwifruit are also high in it. Some vegetable oils, notably soybean contain vitamin K. Menaquinone-4 and Menaquinone-7 (vitamin K\(_2\)) are found in meat, eggs, dairy and natto.
**Deficiency:** Average diets are usually not lacking in vitamin K and its primary deficiency is rare in healthy adults. Its deficiency can be observed in individuals who suffer from liver damage or disease (i.e. Alcoholics), people with cystic fibrosis, inflammatory bowel diseases or those who have recently had abdominal surgeries. Groups which may suffer from its secondary deficiency include bulimics, those on stringent diets and those taking anti-coagulants. Salicylates, barbiturates and cefamandole also lower the levels of vitamin K.

**Water-soluble:** Seven water-soluble vitamins which were analyzed in this part of work were vitamin C and six B-complex vitamins: B1 (Thiamin), B2 (Riboflavin), B3 (Nicotinic acid), B6 (Pyridoxine), B9 (Folic acid) and B12 (Cyanocobalamin). These are readily excreted from the body to the degree that urinary output is a strong predictor of vitamin consumption \[^{38}\]. Because all B-complex vitamins except B12 are not readily stored, consistent daily intake is important. These are more easily destroyed during cooking than fat-soluble vitamins. Proper storage and preparation of food can minimize vitamin loss-refrigeration of the freshly prepared food. An excess of these would not result in any side effects as they will disperse in the body fluids and voided in the urine. The solubility of a vitamin influences the way it is absorbed, transported, stored and excreted by the body. With the exception of vitamin B12 which is supplied by only foods of animal origin, the rest of the vitamins are synthesized by plants.

**Vitamin C or Ascorbic acid:** It is an essential nutrient for humans. Molecular formula of ascorbic acid is C6H8O6. Its IUPAC name is 2-oxo-L-threo-hexono-1, 4-lactone-2, 3-enediol. Ascorbate is required for several metabolic reactions in all animals and plants. Deficiency in this vitamin causes scurvy in humans \[^{P-R/824}\]. It is also widely used as a food additive.

Ascorbate is an anti-oxidant \[^{88}\] and it is a cofactor for several vital enzymatic reactions. Structure of vitamin C is shown in Figure 05.

High vitamin C intake reduces serum uric acid levels and it is associated
with lower incidence of gout syndrome \([P-R/B5]\). It has also been promoted as an effective agent against a vast array of diseases and syndromes - common cold \([P-R/B16, P-R/B36]\), pneumonia \([P-R/B23]\), bird flu, SARS \([44]\), heart disease \([P-R/B21]\), AIDS \([P-R/B5, P-R/B34]\), autism \([P-R/B10]\), low sperm count \([1]\), age-related macular degeneration \([35, P-R/B18]\), altitude sickness \([P-R/B2]\), amyotrophic lateral sclerosis \([P-R/B35]\), asthma \([P-R/B24]\), tetanus \([P-R/B22]\) and cancer \([126]\).

**Forms:** Different forms of this vitamin include: Ascorbic acid which is the pure form with sharp taste and ascorbate bounded with calcium & magnesium which are non acidic forms. Ascorbate is given as a supplement of calcium and magnesium.

**Functions:** It is an effective antioxidant lessening oxidative stress and it is a cofactor for the synthesis of many important cellular compounds. The vitamin acts as an electron donor for 8 different enzymes \([P-R/B29]\):

- Three participate in collagen hydroxylation \([59, 94, 100]\) which allow the collagen molecule to assume its triple helix structure and making vitamin C essential to the development and maintenance of scar tissue, blood vessels and cartilage.
- Two are necessary for synthesis of carnitine \([30, 103]\) which is essential for the transport of fatty acids into mitochondria for ATP generation.
- The remaining 3 have the following functions in common but do not always do this:
  - Dopamine β hydroxylase participating in the synthesis of norepinephrine from dopamine \([57, 66]\).
  - Another enzyme adds amide groups to hormones for increasing their stability \([12, 33]\).
  - One modulates tyrosine metabolism \([34, 68]\).

**Sources:** Plants are generally good sources of vitamin C, particularly rose hips, camu camu fruit, kakadu plum,acerola, seabuckthorn, jujube, indian gooseberry, baobab, black currant, red pepper, parsley, guava, kiwi fruit, broccoli, logan berry, red currant, brussels sprouts, wolf berry, lychee, papaya, strawberry, orange, lemon, melon, cauliflower, garlic, grape fruit, rasp berry, spinach, cabbage, lime, mango, black berry, potato, cran berry,
tomato, blue berry, pine apple, apricot, watermelon, banana, carrot, crab apple, cherry, peach, apple, beet root, peer, cucumber and fig.

Meat, liver, heart and milk are also good sources of vitamin C.

**Deficiency:** Scurvy is due to lack of vitamin C. Without this vitamin, the synthesized collagen is too unstable to perform its function. This leads to the formation of liver spots on the skin, spongy gums and bleeding from all mucous membrane. The spots are most abundant on the thighs, legs and a person with the ailment looks pale, feels depressed and partially immobilized\[^{[P-R/B41]}\]. In advanced scurvy, there are open, suppurating wounds and loss of teeth and eventually death. It has been shown that smokers who have diets poor in vitamin C are at a higher risk of lung-borne diseases than those smokers who have higher concentrations of vitamin C in the blood \[^{[P-R/B38]}\].

**Vitamin B\(_1\):** Vitamin B\(_1\) is also called as thiamine. It is a colorless compound with a molecular formula C\(_{12}\)H\(_{17}\)N\(_4\)O\(_3\). Its IUPAC name is 2\-\[(4\-amino-2\-methyl\-pyrimidin-5\-yl) methyl\]-4\-methyl\-thiazol-5\-yl\] ethanol. It is stable at acidic pH and frozen storage. It is unstable in alkaline solution, when exposed to heat and U.V light or \(\gamma\)-irradiation. It reacts strongly in Maillard-type reactions. The chemical structure of thiamine is shown in Figure 06. It is best known for its role as a cofactor, thiamine diphosphate (ThDP), in many enzymes and multienzyme complexes \[^{[36]}\]. It is transport form of the vitamin, while the active forms are phosphorylated thiamine derivatives. The majority of thiamine in serum is bound to proteins, mainly albumin. Approximately 90\% of total thiamine in blood is in erythrocytes.

**Forms:** There are 4 natural thiamine phosphate derivatives: thiamine monophosphate (ThMP), thiamine diphosphate (ThDP), also known as thiamine pyrophosphate (TPP) or cocarboxylase, thiamine triphosphate (ThTP) and recently discovered adenosine thiamine triphosphate (AThTP) or thiaminylated adenosine triphosphate.
**Functions:** Thiamine derivatives and thiamine-dependent enzymes are present in all cells of the body. They have essential metabolic roles in carbohydrate and protein metabolism and also in neural functions.

- ThDP is a coenzyme for several enzymes that catalyze the transfer of 2-carbon units, particularly in dehydrogenation (decarboxylation and subsequent conjugation with coenzyme A) of 2-oxoacids (α-keto acids).
- Thiamine triphosphate (ThTP) is a specific neuroactive form of thiamine.
- Thiamine is released by the action of phosphatase and pyrophosphatase in the upper small intestine.

**Sources:** Thiamine is found in yeast and pork meat. Cereal grains are the most important dietary sources especially whole grains contain more thiamine than refined grains. It is higher in outer layers of the grain and germ of cereals. In addition to the above yeast, oatmeal, flax, brown rice, whole grain flour (rye or wheat), asparagus, kale, cauliflower, potatoes, oranges, pork, liver (beef or pork) and eggs are the foods rich in thiamine.

**Deficiency:** It is present in all cells of the body and its deficiency would adversely affect all organ systems. Its deficiency leads to neurodegeneration, wasting and death and chronic diseases, such as consumption of alcohol, gastrointestinal diseases, H.I.V-AIDS and persistent vomiting.

Well-known syndromes caused by its deficiency includes BeriBerri and Wernicke - Korsakoff syndrome, a striking neuro-psychiatric disorder characterized by paralysis of eye movements, abnormal stance, gait and markedly deranged mental function which is common with chronic alcoholism \(^{[73]}\). In less severe deficiency, nonspecific signs include malaise, weight loss, irritability and confusion.

**Vitamin B\(_2\):** It is called as riboflavin, the name comes from “ribose” and "flavin". The molecular formula of riboflavin is C\(_{17}\)H\(_{20}\)N\(_4\)O\(_6\) and its IUPAC name is 7,8-dimethyl-10-((2R, 3R, 4S)-2, 3, 4, 5-tetrahydroxypentyl)benzo(g)pteridine-2,4(3H,10H)-dione. This vitamin imparts orange color to solid B-vitamin preparations and yellow to vitamin supplement solutions.
Chemical structure of riboflavin is shown in the Figure 07. It is easily absorbed and plays a key role in maintaining health in humans and animals. Riboflavin is the central component of the cofactors FAD and FMN and is required for all flavoproteins. Like the other B complex vitamins, it plays a key role in energy metabolism and required for the metabolism of fats, ketone bodies, carbohydrates and proteins. In the 1920s, vitamin B\(_2\) was thought to be the factor necessary for preventing pellagra.

**Forms:** Vitamin B\(_2\) was originally considered to have two components, a heat-labile vitamin B\(_1\) and a heat-stable vitamin B\(_2\) [P-R/B7].

**Functions:** FMN and FAD function as coenzymes for a wide variety of oxidative enzymes and remain bound to the enzymes during the oxidation-reduction reactions. Flavins can act as oxidizing agents because of their ability to accept a pair of hydrogen atoms. Reduction of isocitrate ring (FMN and FAD oxidized form) yields the reduced forms of the flavoproteins (FMNH\(_2\) and FADH\(_2\)) [P-R/B20]. Flavoproteins exhibit a wide range of redox potential and therefore play a variety of roles in intermediary metabolism [P-R/B20].

**Sources:** Free riboflavin is naturally present in foods along with protein-bound form [P-R/B3]. Bovine milk contains mainly free riboflavin, with a minor contribution from FMN and FAD. It is found naturally in asparagus, bananas, persimmons, okra, chard, cottage cheese, milk, yogurt, meat, eggs and fish. Leafy vegetables, liver, kidneys, wheat bran, legumes such as mature soybeans [P-R/B7], yeast and almonds are good sources of vitamin B\(_2\), but exposure to light destroys riboflavin [P-R/B32].

**Deficiency:** In humans, signs and symptoms of riboflavin deficiency (ariboflavinosis) include cracked and red lips, inflammation of the lining of mouth and tongue, mouth ulcers, cracks at the corners of the mouth (angular cheilitis) and a sore throat. Its deficiency may also cause dry and scaling skin, fluid in the mucous membranes and iron-deficiency anemia. The eyes may also become bloodshot, itchy, watery and sensitive to bright
light. Riboflavin deficiency is classically associated with the oral-ocular-genital syndrome.

Subclinical deficiencies have been observed in women taking oral contraceptives, in people with eating disorders and in disease states such as H.I.V, inflammatory bowel disease, diabetes and chronic heart disease.

**Vitamin B\textsubscript{3}**: Vitamin B\textsubscript{3} is also called as niacin. It is an organic compound with the molecular formula C\textsubscript{6}H\textsubscript{5}NO\textsubscript{2}. Its IUPAC name is nicotinic acid. It is a derivative of pyridine, with a carboxyl group (COOH) at the 3\textsuperscript{rd}-position. The structure of vitamin B\textsubscript{3} is depicted in Figure 08. It prevents the disease pellagra. It has historically been referred to as "vitamin PP."

**Forms**: Other forms of vitamin B\textsubscript{3} include the corresponding amide, nicotinamide ("niacinamide"), where the carboxyl group has been replaced by a carboxamide group (CONH\textsubscript{2}), as well as more complex amides and a variety of esters. The terms niacin, nicotinamide and vitamin B\textsubscript{3} are often used interchangeably to refer to any one of this family of molecules, since they have a common biochemical activity. Niacin is converted to nicotinamide and then to NAD and NADP *in vivo*.

**Functions**: Niacin and nicotinamide are identical in their vitamin activity; nicotinamide does not have the same pharmacological effects of niacin, which occur as side-effects of niacin's conversion. Niacin is a precursor to NAD\textsuperscript{+}, reduced NAD, NADP and reduced NADP which play essential roles in living cells \cite{PRB11}. It is involved in both DNA repair and the production of steroid hormones in the adrenal gland. The vitamin is required for cell respiration and metabolism of carbohydrates, fats and proteins, for proper circulation and healthy skin, functioning of nervous system and normal secretion of bile and stomach fluids. It is used in the synthesis of sex hormones, being a memory-enhancer in the treatment of schizophrenia and other mental illnesses. Nicotinic acid (but not nicotinamide) given in drug dosage improves the blood cholesterol profile and has been used to clear the body of organic poisons like insecticides.
**Sources:** Niacin is essentially found in animal products like meat, liver, heart, kidney, chicken, beef, fish (tuna and salmon), eggs, yeast and dairy products. It is also available in fruits and vegetables like avocados, dates, tomatoes, leaf vegetables, broccoli, carrots, sweet potatoes, asparagus and mushrooms. Even seeds such as nuts, whole grain products, wheat germ, legumes and saltbush seeds contain niacin.

**Deficiency:** Severe niacin deficiency causes pellagra which is characterized by bilateral dermatitis, diarrhoea and dementia. Mild deficiency slows the metabolism, causing decreased tolerance to cold. Niacin synthesis is deficient in carcinoid syndrome because of metabolic diversion of its precursor tryptophan to form serotonin. The shortage of niacin may be indicated with symptoms such as canker sores, depression, diarrhoea, dizziness, fatigue \(^{[96]}\), halitosis, headache, indigestion, insomnia, limb pains, loss of appetite, low blood sugar, muscular weakness, skin eruptions and inflammation.

**Vitamin B\(_6\):** It is also called as pyridoxine. Its molecular formula is \(C_8H_{11}NO_3\) and its IUPAC name 4, 5 - Bis (hydroxymethyl) -2 -methylpyridin -3 -ol. The structure of B\(_6\) is depicted in Figure 09. It is needed for more than 100 enzymes involved in protein and R.B.C metabolism. Nervous and immune systems need vitamin B\(_6\) to function efficiently and it is also required for the conversion of tryptophan to niacin \(^{[P-R/B10]}\).

**Forms:** It exists in 7 forms: Pyridoxine (PN) form that is given as vitamin B\(_6\) supplement, Pyridoxine 5'-phosphate (PNP), Pyridoxal (PL), Pyridoxal 5'-phosphate (PLP) metabolically active form, Pyridoxamine (PM), Pyridoxamine 5'-phosphate (PMP) and 4-pyridoxic acid (PA) catabolite which is excreted in the urine. All forms except PA can be interconverted.

**Functions:** PLP is the metabolically active form of vitamin B\(_6\) which involves in many aspects of macronutrient, amino acid, glucose and lipid metabolisms, in the synthesis of neurotransmitter, histamine synthesis, gene expression and hemoglobin synthesis. It also helps to increase the amount of oxygen carried by hemoglobin and helps to maintain healthy
lymphoid organs (thymus, spleen and lymph nodes). It generally serves as a coenzyme for many reactions and can help to facilitate decarboxylation, transamination, racemization, elimination, replacement and B-group inter conversion reactions \[^{[P-R/B10]}\]. Liver is the major site for vitamin B\(_6\) metabolism. It is also necessary for the enzymatic reaction governing the release of glucose from glycogen and helps to maintain normal blood glucose (sugar) level at normal and starvation conditions.

**Sources:** It is widely distributed in foods both in free and bound forms. Good sources include meats, whole grain products, vegetables and nuts. In some foods, cooking, storage and processing may cause loss of more than 50% of vitamin \[^{[P-R/B33]}\]. The loss from plant foods would be minimum during processing as they contain mostly pyridoxine which is more stable than pyridoxal or pyridoxamine found in animal foods. It is found in the germ and aleurone layer of grains and milling results to the reduction of this vitamin in white flour. Freezing and canning are other food processing methods that results in the loss of vitamin B\(_6\) in foods \[^{[107]}\].

**Deficiency:** The classic clinical syndrome for B\(_6\) deficiency is a seborrhoeic dermatitis-like eruption, atrophic glossitis with ulceration, angular cheilitis, conjunctivitis, intertrigo and neurologic symptoms of somnolence, confusion and neuropathy \[^{[P-R/B1]}\]. It can result in a form of anemia that is similar to iron deficiency anemia.

Severe vitamin B\(_6\) deficiency results in dermatologic and neurologic changes, less severe cases present with metabolic lesions associated with insufficient activities of the coenzyme pyridoxal phosphate. The most prominent of the lesions is due to impaired tryptophan-niacin conversion. Its deficiency can also result from impaired transsulfuration of methionine to cysteine. The deprivation of vitamin B\(_6\) results in impaired glucose tolerance \[^{[P-R/B10]}\]. Renal patients undergoing dialysis may experience vitamin B\(_6\) deficiency \[^{[P-R/B6]}\].

**Vitamin B\(_9\):** It is also known as folic acid or folacin. Its naturally occurring form is folate. Molecular formula of folic acid is C\(_{19}\)H\(_{19}\)N\(_7\)O\(_6\) and its IUPAC name is \((2S)\cdot2\cdot[\cdot(4\cdot[[2\cdotaminooxypteridin-6-yl]methyl]amino\cdotphenyl]formamido]pentanedioic\) acid. The chemical structure of folic acid
is depicted in Figure 10. It is essential to numerous bodily functions ranging from nucleotide synthesis to the methylation of homocysteine. It is required during periods of rapid cell division and growth. Both children and adults require folic acid to produce healthy R.B.C and to prevent anemia [P-R/B12].

**Forms:** Vitamin B₉ was represented in two different forms: Folic acid, the synthetic form and the other folate which is the natural form.

**Functions:** Folate is necessary for the production and maintenance of new cells [54]. It is especially important during periods of rapid cell division and growth such as infancy and pregnancy. It is also needed to synthesize DNA bases (thymine and purine bases) and for DNA replication.

Folate may prevent cancer as it is involved in the synthesis, repair and functioning of DNA. Its deficiency, therefore, may result in damage of DNA leading to cancer [48]. It is necessary for fertility in both men and women. In men, it contributes to spermatogenesis. In women, it contributes to oocyte maturation, implantation, placentation, in addition to the general effects of folic acid in pregnancy [112].

Folic acid is an important nutrient for pregnant women to protect against a number of congenital malformations including neural tube defects (NTDs) that result in malformations of the spine (spina bifida), skull and brain (anencephaly) [111].

**Sources:** Leafy vegetables such as spinach, turnip greens, lettuces, dried beans and peas, fortified cereal products, sunflower seeds, certain fruits and vegetables are rich sources of folate. Liver and its products also contain high amounts of folate, as does baker’s yeast.

**Deficiency:** Folate deficiency hinders DNA synthesis and cell division affecting bone marrow and cancer both of which participate in rapid cell division [54]. Since folate deficiency limits cell division, erythropoiesis, production of R.B.C is hindered and leads to megaloblastic anemia which is characterized by large immature R.B.C.
**Vitamin B₁₂**: It is also called as cyanocobalamin which plays a key role in the normal functioning of brain and nervous system and for blood formation. It is involved in the cellular metabolism, affecting DNA synthesis and regulation but also fatty acid synthesis and energy production. Biosynthesis of the complicated structure (Figure 11) of the vitamin can only be accomplished by bacteria but conversion between different forms of the vitamin can be accomplished in the human body. Molecular formula of vitamin B₁₂ is C₆₃H₈₈CON₁₄O₁₄P, IUPAC name is α-(5, 6-dimethylbenzimidazolyl) cobamidcyanide. Its common synthetic form does not occur in nature but is used in many pharmaceuticals, supplements and as food additive, due to its stability and lower cost.

**Forms**: It refers to a group of cobalt-containing vitamer compounds known as cobalamins: these includes cyanocobalamin (an artifact formed as a result of the use of cyanide in the purification procedures), hydroxocobalamin (another medicinal form) and finally, the two naturally occurring cofactor forms of B₁₂: 5-deoxyadenosylcobalamin (adenosylcobalamin—AdoB₁₂), the cofactor of methylmalonyl coenzyme A mutase (MUT) and methylcobalamin (MeB₁₂), the cofactor of 5-Methyltetrahydrofolate-Homocysteine Methyltransferase (MTR).

**Functions**: In humans, only 2 corresponding coenzyme B₁₂ dependent enzymes are known: methylmalonyl coenzyme A mutase (MUT) which uses the AdoB₁₂ form and reaction type 1 to catalyze a carbon skeleton rearrangement. MUT's reaction converts MMl-CoA to Su-CoA, an important step in the extraction of energy from proteins and fats and 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR), also known as methionine synthase. This is a methyl transfer enzyme, which uses the MeB₁₂ and reaction type 2 to catalyze the conversion of the amino acid Hcy (homocysteine) back into Met (methionine).
Sources: It is naturally found in meat (especially liver and shellfish), fish, dairy products, chicken, beef, milk and eggs. Animals obtain it from bacteria which inhabit in a section of the gut which is posterior to the section where B\textsubscript{12} is absorbed. Other sources include nutritional yeast or red star and mushroom, Agaricus bisporus.

Deficiency: Its deficiency leads to the disease pernicious anemia (anemia with bone marrow promegaloblastosis (megaloblastic anemia), gastrointestinal and neurological symptoms), which is an autoimmune disease that destroys parietal cells in the stomach that secrete intrinsic factor which is crucial for the normal absorption of B\textsubscript{12}. Therefore, lack of intrinsic factor, as seen in pernicious anemia causes vitamin B\textsubscript{12} deficiency. Most of "B\textsubscript{12} deficient symptoms" are actually folate deficient symptoms, since they include all the effects of pernicious anemia and megaloblastosis, which are due to poor synthesis of DNA when the body does not have a proper supply of folic acid for the production of thymine. When sufficient folic acid is available, all known B\textsubscript{12} related deficiency syndromes were normalized. Its deficiency can potentially cause severe and irreversible damage, especially to the brain and nervous system. At slightly lower than normal levels, a range of symptoms such as fatigue, depression and poor memory may be experienced \cite{P-R/B13}. Its deficiency can also cause symptoms of mania and psychosis \cite{75, 110}.

Considering the above important functions and roles of vitamins, it is clear that they are pivotal to maintain health in humans and their deficiencies may lead to several diseases or impairments.
The present study is focused at studying the profiles of vitamins in various selected populations with universally prevalent diseases like H.I.V, Coronary artery disease, Diabetes Mellitus, Hyper and hypotension, Tuberculosis and Alzheimer’s. In addition to these, people having unhealthy habits like smoking and consumption of alcohol besides women with specific conditions viz. Menopause and Hysterectomy were included. A brief description of the above diseases/impairments was presented here.

**Human immunodeficiency virus (H.I.V):** It is a lentivirus (member of retrovirus family) which can lead to acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail leading to life-threatening opportunistic infections. Previous names for the virus include human T-lymphotropic virus-III (HTLV-III), lymphadenopathy-associated virus (LAV) and AIDS-associated retrovirus (ARV) [23]. The structure of the virus is depicted in the Figure 12.

The 4 major routes of transmission are unprotected sexual intercourse [67, 122, P-R/B17], contaminated needles [12, 55], breast milk and transmission from an infected mother to the baby [25] (vertical transmission). H.I.V infection occurs by the blood transfusion [28], semen, vaginal fluid, pre-ejaculate and breast milk. H.I.V is present in free state in these body fluids and infected immune cells.

H.I.V primarily infects T-helper cells (specifically CD4+ T cells), macrophages and dendritic cells. This infection lowers the levels of CD4+ T cells through three main mechanisms: a) Direct viral killing of infected cells; b) Increased rates of apoptosis in infected cells; c) Killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4+ T cell numbers decline below a critical level, cell-mediated
immunity is lost and the body becomes progressively more susceptible to opportunistic infections.

**Symptoms:** The early symptoms often include moderate and unexplained weight loss, recurring respiratory tract infections (such as sinusitis, bronchitis, otitis media, pharyngitis), prostatitis, skin rashes and oral ulcerations. Common opportunistic infections and tumors, most of which are normally controlled by robust CD4+ T cell-mediated immunity then start to affect the patient. The common symptoms include fever, lymphadenopathy, pharyngitis, rash, myalgia, malaise, mouth and oesophageal sores, but less common symptoms are headache, nausea, vomiting, enlarged liver/spleen, weight loss, thrush and neurological complications [53].

Eventually most of the H.I.V-infected individuals without treatment develop AIDS. These individuals mostly die from opportunistic infections or malignancies associated with the progressive failure of the immune system [63].

**Coronary Artery Disease (C.A.D):** It is one of the cardiac diseases which involve heart and blood vessels (arteries and veins). It is caused due to the interruption of blood supply to a part of heart, which may ultimately lead to the death of heart cells. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (fatty acids) and white blood cells (especially macrophages) in the wall of coronary artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, can cause damage or death (infarction) of heart muscle tissue (myocardium). Myocardial infarction (MI) is depicted in Figure. 13.

Sudden death from heart...
attack is most often due to an arrhythmia (irregular heartbeat or rhythm) called ventricular fibrillation. If a person survives a heart attack, the injured area of the heart muscle is replaced by scar tissue. This weakens the pumping action of the heart and can lead to heart failure and other complications.

The major risk factors include tobacco smoking, high levels of blood lipids (triglycerides, low-density lipoprotein) and low levels of high density lipoprotein (HDL), diabetes [27], H.T, obesity [127], chronic kidney disease, excessive consumption alcohol, abuse of drugs such as cocaine and methamphetamine and chronic high stress levels [11, 93]. Acute severe infections like pneumonia can trigger myocardial infarction.

**Symptoms:** These include sudden chest pain (typically radiating to the left arm or left side of the neck) prior to the infarction, dyspnea (shortness of breath), nausea, vomiting, palpitations, light headedness, diaphoresis (excessive sweating) and anxiety (sense of impending doom). Women and older people may experience fewer typical symptoms than men [18], most commonly dyspnea, weakness, feeling of indigestion, sleep disturbances and fatigue [61] one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of coronary ischemia than in men [76].

**Diabetes Mellitus (D.M):** It is a metabolic disorder where body does not produce or properly use the hormone insulin produced by the pancreas (Figure. 14). It is characterized by hyperglycemia (high levels of blood glucose) and glucosuria (presence of glucose in urine). So, humans have to maintain glucose levels by insulin regulation in a very narrow range, despite of irregular intervals between the meals with a substantial carbohydrate load. However, blood glucose level may rise temporarily up to 140 mg/dL after taking food in non-diabetics. Several other factors also influence the blood glucose levels such as yeast infections, stress either physical or
psychological and exercise (prolonged or long after recent meal) hormonal imbalance. Glucagon and adrenalin are known to regulate blood glucose levels. The normal range readings of blood glucose levels were given in Table 02.

Blood glucose levels are reported in terms of a molar concentration, measured in mmol/L (millimoles per litre; or millimolar, abbreviated mM) and mass concentration, measured in mg/dL (milligrams per decilitre).

Table 02: Normal range readings of blood glucose level:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Fasting</th>
<th>Post Prandial</th>
<th>Random</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>70 – 110</td>
<td>110 – 140</td>
<td>70 – 125</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>&lt;70</td>
<td>&lt;110</td>
<td>&lt; 140</td>
</tr>
<tr>
<td>Early Hyperglycemia</td>
<td>101 – 126</td>
<td>140 – 200</td>
<td>70 – 140</td>
</tr>
<tr>
<td>Established Hyperglycemia</td>
<td>&gt;126</td>
<td>&gt;200</td>
<td>&gt;140</td>
</tr>
</tbody>
</table>

*All values in milligrams per deciliter (mg/dL) according to 1999 WHO diabetes criteria.

*Fasting: Blood glucose level after an eight hour fast.
*Post Prandial: Blood glucose level within two hours after the meal.
*Random: Blood glucose level throughout the day regardless of having meals.

Though diabetes is not completely curable, it can be controlled to a greater extent by diet, exercise and medication.

**Symptoms:** The temporary elevated blood glucose level may also result from severe stress such as trauma, stroke, myocardial infarction or surgery, illness and other symptoms like polyuria (frequent urination), polydipsia (increased thirst), dry mouth, significant weight loss, polyphagia (increased hunger) [24]. Itchy skin, skin rashes can occur in diabetes that is collectively known as diabetic dermadromes. Blurred vision, leg pains, cuts or sores that are slow to heal are common complaints in diabetes patients.

- Overweight, lack of exercise, family history and stress increase the likelihood of diabetes. Diabetes is a primary reason for adult blindness, end stage-renal disease (ESRD), gangrene and amputations. When blood glucose level is constantly high, appetite is suppressed over the short term leads to complications like cardiovascular disease, kidney failure, eye problems and nerve
damage. People with diabetes are 4 times more likely to have coronary heart diseases and stroke compared to normals.

- Without proper treatment, diabetes may lead to other acute complications like diabetic ketoacidosis or nonketotic hyperosmolar coma. Treatment of diabetes is thus important, as well as controlling hyper and hypotension and lifestyle factors such as smoking cessation and maintaining a healthy body weight.

- People with hypoglycemia report drowsiness or impaired cognitive function due to low blood sugar, several hours after meals. They may also include lethargy, impaired mental functioning, irritability, shaking, twitching, weakness in arm and leg muscles, pale complexion, sweating, paranoid or aggressive mentality and loss of consciousness sometimes brain damage may occur.

**Hyper and hypotension (H.T):** It is the force that exert on the arterial walls as the heart pumps blood throughout the body. The pressure is determined by the force, amount of blood pumped, size and flexibility of the arteries as shown in the Figure 15. Blood pressure reading provides two measures, systolic and diastolic pressures, expressed as millimeters of mercury (mm Hg) in a sphygmomanometer or how high the pressure of blood would raise a column of mercury \(^{[15]}\). The pressure is measured at a person’s upper arm inside of an elbow at the brachial artery, (major blood vessel) which carries blood away from the heart. Systolic pressure is measured as the heart pumps. Diastolic pressure is measured between beats, as blood flows back into the heart. They also change in response to stress, nutritional factors, drugs, disease, exercise and momentarily from standing up, variations are large along with body temperature, respiratory rate and pulse rate.

Factors such as age and gender \(^{[104]}\) influences blood pressure. In children, the normal ranges are lower than for adults and depend on height. In adults, systolic pressure tends to rise and diastolic tends to fall. In aged
persons, blood pressure tends to be higher due to reduced flexibility of the arteries. It also varies with exercise, emotional reactions, sleep, digestion and time of day. Normal range readings were given in Table 03.

Table 03: Normal range readings of hyper and hypo tension:

<table>
<thead>
<tr>
<th>Types of H.T</th>
<th>Systolic (mm Hg)</th>
<th>Diastolic (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>&lt; 90</td>
<td>&lt; 60</td>
</tr>
<tr>
<td>Normal</td>
<td>90 - 120</td>
<td>60 - 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 - 139</td>
<td>80 - 89</td>
</tr>
<tr>
<td>Hypertension – stage 1</td>
<td>140 - 159</td>
<td>90 - 99</td>
</tr>
<tr>
<td>Hypertension – stage 2</td>
<td>≥ 160</td>
<td>≥ 100</td>
</tr>
</tbody>
</table>

*Based on two readings taken 5 min apart with a confirmation reading in the contra lateral arm. R/B14.

Hypotension is due to low blood pressure. It is a medical concern only if arterial pressure and blood flow decrease beyond a certain point, the perfusion of the brain becomes critically decreased (lack of blood supply), causing lightheadedness, dizziness, weakness or fainting. Causes of low arterial pressure include sepsis, hemorrhage, toxins and hormonal abnormalities such as Addison's disease.

Orthostatic hypotension (pht) fall in arterial pressure is observed in some persons when they standing from sitting position as gravity reduce the rate of blood return from the body veins, below the heart and back to the heart, thus reducing cardiac output.

Hypertension is silent killer because it has no symptoms and can go undetected for years and it cannot be cured, but controlled through lifestyle changes and prescriptive medication.

**Symptoms:** Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm and is a leading cause of chronic renal failure. Even moderate elevation of arterial H.T leads to shortened life expectancy. The risk of cardiovascular disease (CVD) increases progressively above 115/75 mmHg. CVD risk doubles for each increment of 20/10 mmHg. All levels of arterial pressure put mechanical stress on the arterial walls. Higher pressures increase heart workload and progression of unhealthy tissue growth (atheroma), which develops within
the walls of arteries. This leads to heart muscle thickening, enlargement and weaker over time.

**Tuberculosis (T.B):** It is a common and deadly infectious disease caused by *Mycobacterium tuberculosis* [P-R/B26]. It is associated with poverty, overcrowding, consumption of alcohol, stress, drug addiction and malnutrition. It usually attacks the lungs but can also affect other parts of the body. It spreads easily in overcrowded, badly ventilated places and under nourished people, through the air, when people who have the disease cough, sneeze or spit [P-R/B25]. Most of the infections result in an asymptomatic, latent infection and about one in ten latent infections eventually progresses to active disease, which if left untreated kills more than 50% of its victims.

One third of the world’s population is thought to be infected with *M. tuberculosis* in causing pulmonary tuberculosis as shown in Figure 16 and new infections occur at a rate of about one per second. The proportion of people who become sick with tuberculosis each year is stable or falling worldwide but due to population growth the number is still increasing [P-R/B39]. In addition, more people in the developed world are contracting tuberculosis because their immune systems are compromised by immunosuppressive drugs, substance abuse or AIDS.

**Symptoms:** The classic symptoms are a chronic cough with blood-tinged sputum, fever, night sweats and weight loss. Infection of other organs causes a wide range of symptoms.

- Pulmonary T.B has chest pain and severe cough, sometimes with blood in the sputum. Systemic symptoms include fever, chills, night sweats, appetite loss, weight loss, pallor and often a tendency to fatigue very easily.

- In extra-pulmonary T.B which occurs more commonly in immuno suppressed persons and young children [P-R/B18], the sites of infection
includes pleura in tuberculosis pleurisy, central nervous system in meningitis, lymphatic system in scrofula of the neck, genitourinary system in urogenital tuberculosis and bones and joints in Pott's disease of the spine.

Extra-pulmonary T.B may co-exist with pulmonary T.B as well; whose symptoms are weight loss, exhaustion, night sweats and fever.

**Alzheimer's disease (A.D):** It is the most common form of dementia. This is incurable, degenerative and terminal disease, first given by Alois Alzheimer in 1906 and was named after him. It is a neurodegenerative illness characterized by a gradual decline in memory, cognitive and behavioral abilities, leading to occupational and social impairment. Generally, it is diagnosed in people over 60 yrs of age even though it is less-prevalent. Alzheimer's can occur much earlier. Other possible risk factors include low education level, history of head trauma, female gender and cardiovascular disease. Aluminum exposure has also been proposed as a potential contributor.

This disease damages areas of the brain involved in memory, intelligence, judgment, language and behavior as illustrated in Figure 17. It not only affects memory but also behavior, personality, ability to think and ability to function from day to day.

**Symptoms:** Even though Alzheimer’s disease is unique for every individual, there are many common symptoms. The earliest ones are often mistakenly thought to be 'age-related' concerns or manifestations of stress. In the early stages, the most commonly recognized symptom is memory loss, such as difficulty in remembering recently learned facts.

As the disease advances symptoms include confusion, irritability, aggression, mood swings, language breakdown, long-term memory loss and general withdrawal of the sufferer as their senses decline. Gradually, bodily functions are lost, ultimately leading to death.
Unhealthy Habits: It means being abnormally tolerant to and dependent on something that is psychologically or physically habit-forming (especially consumption of alcohol and smoking). A habit of smoking and heavy drinking may predispose individuals to make poor food choices and increase their health risks. The combination of smoking, liberal drinking and poor nutrition conceivably elevates the risk for various chronic diseases such as cancer and cardiovascular disease.

Smoking of tobacco (contains nicotine) and consumption of alcohol are interrelated with each other. It is found that heavy drinking is common in current smokers than former or nonsmokers. While the combination of smoking and drinking was not more potent than either behavior alone, both exerted a negative effect on eating habits that corresponded to drug dosage. In other words, as the number of daily cigarettes and alcohol drinks increased, the intake of nutritious grains, fruits and vegetables decreased.

Symptoms: Smoking of tobacco leads to dependence on nicotine. Although smoking is best known for causing lung cancer which is depicted in Figure 18, it also causes threats to the skin next to sun and chemicals which include natural aging process and narrowing of blood vessels throughout the body, including the supply to outermost layers of the skin with oxygen and nutrients.

Consumption of alcohol also has similar effect on the body by destroying the supply of antioxidants. On the other hand, drinking liquor tends to expand blood vessels causing red spots and itchiness on the skin. Women who regularly consume low to moderate amounts of alcohol have an increased risk of cancers of the upper digestive tract, rectum, liver, pancreatic and breast.

Short-term effects of consumption of alcohol include intoxication which effects the brain, causing slurred speech, clumsiness and delayed reflexes, along with dehydration and ultimately alcohol poisoning.
Long-term effects include changes in digestion, alterations in metabolic functions of liver and brain, addiction and alcohol-related dementia called Wernicke-Korsakoff syndrome. Moderate consumption of alcohol has been linked with different types of cancers like mouth, pharyngeal, oesophageal, laryngeal, breast, bowel, pancreatic and liver. Heavy drinkers are more likely to develop liver cancer due to cirrhosis of the liver as shown in the Figure 18.

**Menopause (M.C):** It is opposite to menarche which is the permanent cessation of menstruation (menstrual cycles) which occurs for a considerable length of time before the end of the lifespan. In adult females, menopause starts when the functioning of the ovaries begin to change. It usually happens more or less in midlife, signaling the end of the fertile phase of a woman’s life. However, menopause in women cannot satisfactorily be defined simply as the permanent “stopping of the monthly periods” because in reality what is happening to the uterus is quite secondary to the process and it is what is happening to the ovaries that are the crucial factors as shown in Figure 19.

In females who are not pregnant or lactating, menopause is identified by a permanent (at least one year’s) absence of monthly periods or menstruation. Decrease in the levels of circulating estrogen impacts the entire cascade of a woman’s reproductive functioning, from brain to skin.

The typical age range for the occurrence of menopause is between the ages of 45 to 55 yrs which varies according to geographic location. However, menopause is usually not used to refer to one day, but to the whole of the menopause transition years. This span of time is also referred to as the change of life, the change or the climacteric and more recently is known as peri menopause (around menopause). Menopause is often used to mean all the years of post menopause.
During peri menopause, the production of most of the reproductive hormones including the estrogens, progesterone and testosterone diminish and become more irregular, often with wide and unpredictable fluctuations in levels. In the peri menopause years, many women undergo significant bodily changes resulting from hormonal fluctuation.

Post menopause is a period in woman’s life that takes place after her last period ever or the point when her ovaries become inactive. A woman can be declared to be in post menopause once she has gone 12 full months with no flow at all, not even any spotting. After one year of post menopause period, woman is considered infertile and no longer needs to be a factor in the possibility of becoming pregnant. This is a natural life change but not a disease state or a disorder.

**Symptoms:** In the females, decreased estrogen levels are found in the body and their protection for long bones (as padding) decreases. This increases the risk of osteoporosis. The other symptom of menopause is hot flash (sudden increase in body temperature) caused by declining estrogen levels. Most of the women will gain weight, especially in the lower abdomen, buttocks and thighs. Some of these complaints may not be related to the actual hormonal fluctuations involved in menopause.

**Hysterectomy (H.C):** It is the surgical removal of uterus in reproductive aged women. In younger woman, periods will cease permanently and she will be technically infertile, but as long as at least one of her ovaries is still functioning, the woman will not reach menopause; even without the uterus, ovulation and the release of the sequence of reproductive hormones will continue to cycle till menopause is reached. But in circumstances when a woman’s ovaries are removed (oophorectomy), even if the uterus were to be left intact, the woman is said to be in surgical menopause state.
Hysterectomy at menopause might be done because of persistent bleeding. It can be performed in several ways, through the vagina or abdominal wall, using traditional or laparoscopic techniques. It may be total (removing the body of uterus, fundus and cervix), partial (removal of the uterine body but leaving the cervical stump, also called subtotal) and radical (removal of the uterus, cervix, upper vagina and parametrium). Sometimes lymph nodes, ovaries and fallopian tubes are also removed. However, the types of hysterectomy are depicted in the Figure 20.

Most common risks associated with hysterectomy are serious which includes blood clots, infection, excessive bleeding, urinary tract and bladder or rectum damage during surgery, premature menopause, bowel blockage and adverse reaction to anesthesia.

In some conditions, hysterectomy is the only true cure for some disorders like premalignancies, endometriosis, adenomyosis, prolapsed uterus, excessive uterine fibroids or benign tumors in the uterus and chronic pelvic pain.

**Symptoms:** Estrogen levels fall sharply when hysterectomy is performed and the protective effects of estrogen on the cardiovascular and skeletal systems are lost. It is substantially different from a naturally occurring menopausal state; the former is a sudden hormonal shock to body that causes rapid onset of menopausal symptoms while the latter is a gradually occurring decrease of hormonal levels over a period of years with uterus intact and ovaries able to produce hormones even after the cessation of menstrual periods.

If only uterus is removed, there is three times greater risk of cardiovascular disease. If the ovaries are removed, the risk is seven times greater. It is also associated with osteoporosis and increased risk of bone fractures.

For the purpose of present study, in order to understand vitamin profiles in diverse pathological and specified conditions, following urban and rural areas of East Godavari district in Andhra Pradesh, India were selected.
<table>
<thead>
<tr>
<th>S. No</th>
<th>Location</th>
<th>Urban / Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Narayananapuram</td>
<td>Urban</td>
</tr>
<tr>
<td>2</td>
<td>Lakshminarapupeta</td>
<td>Urban</td>
</tr>
<tr>
<td>3</td>
<td>Gorakshanapeta</td>
<td>Urban</td>
</tr>
<tr>
<td>4</td>
<td>Danaviapeta</td>
<td>Urban</td>
</tr>
<tr>
<td>5</td>
<td>Thumalluva</td>
<td>Urban</td>
</tr>
<tr>
<td>6</td>
<td>Gurunanaknagar</td>
<td>Urban</td>
</tr>
<tr>
<td>7</td>
<td>Aliquot-gardens</td>
<td>Urban</td>
</tr>
<tr>
<td>8</td>
<td>Nehrunagar</td>
<td>Urban</td>
</tr>
<tr>
<td>9</td>
<td>Symalanagar</td>
<td>Urban</td>
</tr>
<tr>
<td>10</td>
<td>Rajanagaram</td>
<td>Rural</td>
</tr>
<tr>
<td>11</td>
<td>Diwancheruvu</td>
<td>Rural</td>
</tr>
<tr>
<td>12</td>
<td>Srimapuram</td>
<td>Rural</td>
</tr>
<tr>
<td>13</td>
<td>Dosakayalapalli</td>
<td>Rural</td>
</tr>
<tr>
<td>14</td>
<td>Velugubanda</td>
<td>Rural</td>
</tr>
<tr>
<td>15</td>
<td>Bommuru</td>
<td>Rural</td>
</tr>
<tr>
<td>16</td>
<td>Dhavaleshwaram</td>
<td>Rural</td>
</tr>
<tr>
<td>17</td>
<td>Kadiyam</td>
<td>Rural</td>
</tr>
</tbody>
</table>

In order to understand the details of their clinical condition which includes blood group with Rh factor, hemoglobin and hematocrit percentages were collected. In addition to the above, survey has been conducted related to their economic standards and occupations besides their vitamin supplementation.

For further execution of the study, it is aimed to optimize the analyzed serum vitamin concentrations by using non-linear statistical data modeling tool Artificial Neural Networks (ANN) or Neural Networks (NN). It offers a new dimension for the present study due to its unique advantages such as nonlinear processing capacity and ability to model poorly understood biological system. It is suitable for simulation and optimization for the exact study of systems from all points of view, without performing additional experiments. A brief description to ANN was included here.

**Artificial Neural Network (ANN):** It is a mathematical or computational model inspired by biological neural network system which consists of neurons and their axons, dendrites and synapses. Similarly, ANN consists of a network of simple processing elements (PEs) also called as neurons, nodes or units, which exhibits complex global behavior, determined by the
connections between the nodes and element parameters [P-R/B21]. In most cases, ANN changes its structure based on external or internal information that flows through the network during the learning phase (adjustment of flow of information for desired output). They can be used to model complex relationships between inputs and outputs or to find patterns in data. In common, its principle is of non-linear, distributed, parallel, global and local processing.

Neural networks or parts of neural networks (such as artificial neurons) are used as components in larger systems that combine both adaptive and non-adaptive elements. The approach of such adaptive systems is suitable for real-world problem solving. ANN is an adaptive and nonlinear system that learns to perform a function (an input/output) from data. Adaptive means the system parameters are changed during the operation (training phase). After the training phase, ANN parameters are fixed and the system is deployed to solve the problem at hand (testing phase). ANN is built with a systematic step-by-step procedure to optimize a performance criterion or to follow some implicit internal constraint (learning rule). The input/output training data are fundamental in ANN technology because they convey the necessary information to discover the optimal operating point. The nonlinear nature of ANN nodes provides the system with lots of flexibility to achieve practically any desired input/output.

ANN with its remarkable ability to derive meaning from complicated or imprecise data can be used to extract patterns and detect trends that are too complex to be noticed by either humans or other computer techniques. A trained ANN is thought as an expert in the category of information it has been given to analyze. Other advantages of it include:

- Adaptive learning: An ability to learn how to do tasks based on the data given for training or initial experience.
- Self-Organization: ANN can create its own organization or representation of the information it receives during learning time.
• Real Time Operation: ANN computations may be carried out in parallel and special hardware devices are being designed and manufactured which take advantage of this capability.

• A neural network can perform tasks that a linear program cannot.

• When an element of the neural network fails, it can continue without any problem by their parallel nature.

• A neural network learns and does not need to be reprogrammed.

**Artificial Neural system:** In this system, the complexity of biological neuron is highly abstracted while modeling artificial neuron (Figure 21) which is a device with many inputs (like synapses) which are multiplied by weights (strength of the respective signals) and then computed by a mathematical function (activation function) which determines the activation of the neuron. Another function (which may be the identity) computes the output of the neuron (sometimes in dependence of a certain threshold. In mathematical terms, the neuron activates if and only if;

\[ X_1W_1 + X_2W_2 + X_3W_3 + ... > T \]

Where, \( X_1, X_2, X_3 \ldots X_n \) are the inputs to the neuron;

\( W_1, W_2, W_3 \ldots W_n \) are the respective weights for the inputs and \( T \) is the pre-set threshold value.

Higher a weight of a neuron is the stronger input, which is multiplied by it will be. Negative weights will inhibit the signals of neuron. Depending on the weights, the computation of the neuron differs and adjusting the weights, desired output is obtained for specific inputs. If ANN has more number of neurons, it becomes quite complicated to find all weights by hand. At this condition, ANN uses an algorithm for adjusting the weights to obtain the desired output from the network. This process of adjusting the weights is called learning or training. Several algorithms exist, but the most used ones are the Delta rule and the back error propagation.
The former is used in feed-forward networks and the latter in feedback networks.

ANNs connects the neurons to process information, which has two modes of operation; the training and testing mode. In the training mode, the neuron is activated, for particular input patterns. In the testing mode, when a taught input pattern is detected at the input, its associated output becomes the current output. If the input pattern does not belong in the taught list of input patterns, the learning rule is used to determine whether to activate or not.

‡ **ANN Topologies:** The pattern of connections between the neurons and propagation of data is collectively considered as ANN topology. It is of two types:

‡ **Feed-forward Networks:** It is also called as bottom-up or top-down, where the signal from input to output neurons is strictly forward (one way). It is depicted in the Figure. 22 The data processing can extend over multiple (layers of) neurons, but no feedback connections are present, i.e., connections extending from output to input neurons in the same layer or previous layers. It is extensively used in pattern recognition.

‡ **Feedback Networks:** This is also called as interactive or recurrent architecture which contains feedback connections where the signal travels from input to output neurons and vice-versa shown in Figure. 23. It is dynamic i.e., changes its state to reach an equilibrium point. This is maintained until the input changes and a new equilibrium is needed. It is very powerful and extremely complicated. In some cases, the activation values of the neurons undergo a relaxation process such that the ANN will evolve to a stable
state in which these activations do not change anymore\textsuperscript{[92]}.

\section*{Training of ANN:} ANN has to be configured such that the application of a set of inputs produces (either 'direct' or via a relaxation process) the desired set of outputs. Various methods to set the strengths of the connections exist. One way is to set the weights explicitly, using a priori knowledge. Another way is to 'train' the neural network by feeding it teaching patterns and letting it change its weights according to some learning rule.

There are three major training patterns, each corresponding to a particular abstract learning task. These are supervised learning, unsupervised learning and reinforcement learning. Usually any given type of network architecture can be employed in any of those tasks.

We can categorize the learning patterns in three distinct sorts. These are:

- **Supervised or Associative learning:** In which the network is trained by providing it with input and matching output patterns. These input-output pairs can be provided by the system which contains the neural network (self-supervised) which finds the function to match the input-output pairs. This function is commonly mean-squared error which minimizes the average squared error between the network’s output and target output. Gradient descent function is used in back propagation algorithm for training neural networks.

- **Unsupervised or Self-organized learning:** In which an (output) unit is trained to respond to clusters of pattern within the input. In this paradigm the system is supposed to discover statistically salient features of the input population. Unlike the supervised learning paradigm, there is no a priori set of categories into which the patterns are to be classified; rather the system must develop its own representation of the input stimuli. This paradigm is generally used for estimation problems, clustering and estimation of statistical distributions.

- **Reinforcement Learning:** This type of learning may be considered as an intermediate form of the above two types of learning. Here input data is not given, but generated by an agent’s interactions with the environment.
and gets a feedback response from the environment. The learning system grades its action according to some unknown dynamics (but are estimated) based on the environmental response and accordingly adjusts its parameters. Generally, parameter adjustment is continued until an equilibrium state occurs, following which there will be no more changes in its parameters. Tasks that fall within the paradigm are control problems, games and other sequential decision making tasks.

**Applications:** ANN tends to refer mostly to neural network models employed in statistics, marketing, medical and clinical diagnosis, data processing, process control, cognitive psychology and artificial intelligence.

* Statistics: Function approximation or regression analysis including time series prediction, fitness approximation and modeling.
* Marketing: To predict the movement of stocks currencies etc., from previous data.
* Medical diagnosis: Assisting doctors with their diagnosis by analyzing the reported symptoms, detection and evaluation of medical phenomena.
* Clinical diagnosis: To estimate tumor sizes, H.T., blood sugar and physical data (age, sex, body temperature, breathe and heart rate), physiological data, usage of drugs and other therapies and laboratory results.
* Data processing: Filtering, clustering, blind source separation and compression of data.
* Process Control: To improve the process reproducibility, productivity and product yield by online response and self tuning.
* Cognitive psychology: Classification including pattern and sequence recognition, novelty detection and decision making.
* Artificial intelligence: Robotics including directing manipulators, computer numerical control and signature analysis.