



Evaluation of iron, electrolytes (sodium, potassium, and chloride) levels in human males suffering from low testosterone

Mohammed Hasan Barrak¹, Inas Hazim Hameed², Farah Ali Dawood¹

¹ University of Mustansiriya, College of Dentistry, Iraq

² Tikrit university, college of science, Iraq

Email: enashazim@uomustansiriyah.edu.iq

DOI:10.21608/jbaar.2024.313562.1070

Abstract

Spermatogenesis, male sex characteristics, sex differentiation, and fertility are all regulated by testosterone, the primary hormone in males. Many organ systems are affected by low testosterone in men. Reduced testosterone has physiological effects on men's health, including mood, cognitive function, muscle mass and strength, and bone density. A differential diagnosis is made using the patient's medical history of the patient, physical examination, clinical symptoms, and testosterone levels. An iron deficit is brought on by iron loss through blood loss or other disorders, and anemia is the result. electrolytes are present in the extracellular and intracellular fluids. In the extracellular fluid, sodium and chloride are the main cations and anions. In the intracellular fluid, potassium is the primary cation. Preserving homeostasis requires electrolytes.

Keywords: Iron, testosterone, potassium, sodium, chloride.

1- Introduction

1-1. Testosterone

In men, the testes are the primary contributor to testosterone, the most popular androgen. The adrenal glands outside the ovaries convert the mini amounts of androgen forerunner produced by the women's ovaries into testosterone, both sexes share this. Adult males have 15-25 times more testosterone in their blood than females do; the production of sperm, the general expansion and development, and the prevention of osteoporosis are all dependent on the presence of this chemical [1]. The free hormone hypothesis proposes that the activity of hormones and associated physiological changes are derived from the free part of the hormone that is not bound in the circulation [2]. The concentrations of testosterone in men and the sexual functioning of the elderly are reduced with age; diseases and conditions that are metabolic may contribute to this process [3].

The contrasting intramural element of the virile procreative arrangement becomes evident during the first seven to ten weeks of development, and this is dependent on testosterone. Throughout juvenility, androgens affect height, the production of sperm, the growth of preoccupation, and the physical characteristics unique to men. A decrease in libido, as well as a decrease in the density of bones, muscles, erythropoiesis, and the size of the male gonad, is attributed to an increase in fat production when testosterone levels decrease with age. Additionally, testosterone promotes anabolic processes in the body and affects the creation of proteins in skeletal muscle [4]. It additionally causes modification in the level of enzymes involved in myocyte transformation and speeds up the restoration of normal tissue composition following exercise [5]. In muscle tissues, testosterone increases the number of planetoid cells and nuclei in the

myocytes [6]. The composition of testosterone is illustrated in Figure 1.

The Leydig cell is primarily involved in creating testosterone in the testis. The manufacturing of testosterone is important to the creation of the

intrinsic and outermost genitals of men, the development of additional traits, and the creation of sperm. Figure 2 depicts how Leydig cells produce testosterone as well as other androgens, the procedure involves different methods of cholesterol creation.

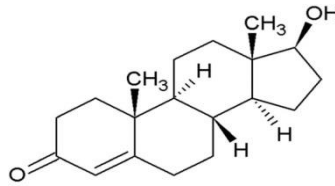


Figure 1: Structure of testosterone [7].

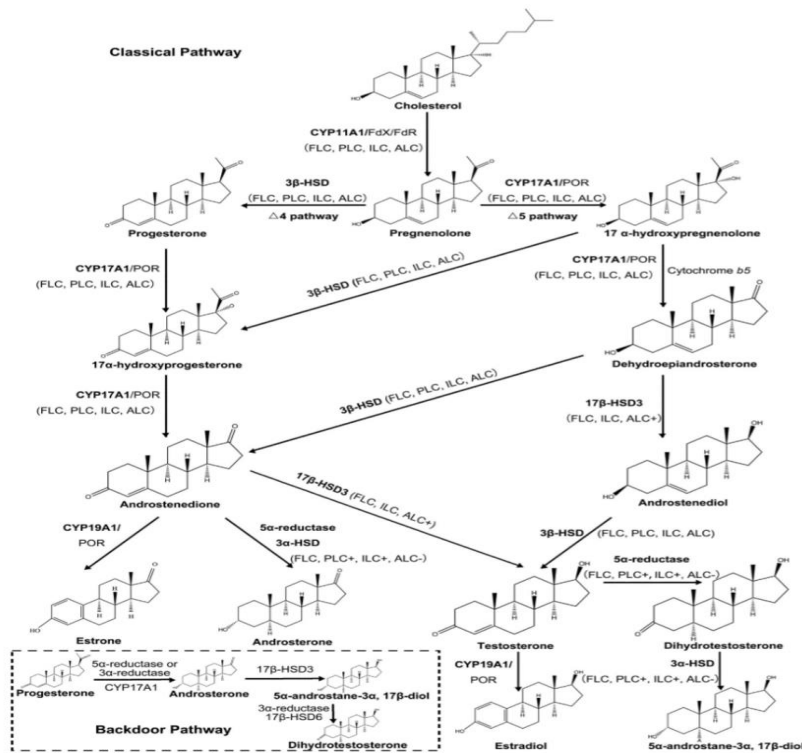


Figure 2: Lesydig cell testosterone metabolism and biological processes [8].

1-2 Iron

Iron is one of the most common elements on Earth and is vital to the majority of living things [9]. One of the most important inorganic components of biology that have an impact on multitudinous biological mechanisms in the individual body is iron, these processes include metabolism, immunological response, the creation of heme, the transport of oxygen, the respiration of cells, the conception of DNA and RNA, and detoxification. Healthy cells have a mechanism that actively changes the amount of iron in their protoplasm via cellular storage and intake, system-wide transportation, and absorption [10]. Serum ferritin is an iron storage protein with the primary role of regulating cellular oxygen metabolism [11]. Iron is crucial to the activeness of numerous biological molecules that are involved in contrasting processes, including the synthesis of hemoglobin, the migration of oxygen throughout the body, furthermore the catalytic role of various enzymes [12]. The equilibrium of iron is maintained by the stomachic cells that are involved in iron absorption, as well as the liver's parenchyma and the mobilization of macrophages. Iron is essential to the transportation of oxygen because it is part of the hemoglobin molecule. The iron levels in the human body are specifically disciplined; the typical concentration is around 40 mg/kg for women and 50 mg/kg for men [13]. The eradication of every form of bodily iron, especially from hepatocytes and macrophages, is called iron deficiency. Since the majority of iron is involved in the creation of Hb, it produces 200 billion red blood cells every day, this is the most obvious sign of iron deficiency. Iron deficiency anemia is frequently misdiagnosed as iron deficiency. However, the term "iron deficiency" is more general and typically refers to a deficiency in other organs and tissues besides the heart, the term is also associated with an earlier onset of anemia, such as the muscles, which require iron in large quantities to produce myoglobin and the energy necessary to force the heart to contract [14].

1-3 Electrolytes

Electrolytes are substances that allow for the transmission of electricity when imbibed in a water-based solvent. Many biological processes are dependent on them, including maintaining a sufficient amount of water, sending nerve signals, and controlling the pH of the water. Among the alimentary substances and beverages that contain electrolytes are sports drinks, fruits, vegetables, and supplements. Electrolytes have a significant impact on maintaining water levels. For the water to remain in the tissues and cells of the body, which comprise the majority of blood, electrolytes are important. The three main electrolytes that the body needs to have a water balance are sodium, potassium, and chloride. Potassium is the primary electrolyte in cells, while sodium is the primary electrolyte outside of them. Outside of the cell, chloride is important for maintaining electrolyte balance in the body and maintaining fluid stability [15,16]. The three principal electrolytes are chloride, potassium, and sodium.

1-3-1 Potassium

As the primary electrolyte in cells, potassium is considered a macroelement that maintains the cell's osmolality and base of pH, it communicates with the brain and regulates the heart and muscle [17]. Through paracellular transport, the intestinal cells in the larger intestine have a high degree of efficiency and precision (90%) [18]. The amount of potassium that is absorbed orally and through the intestines is somewhat different, and the capacity to absorb potassium decreases when magnesium is lacking [19]. Cells represent about 98% of the total amount of potassium in the adult human body, and this amount usually ranges between 3000 and 3500 mmol [20]. The kidneys regulate the amount of potassium that enters and exits the body and maintain a balance of potassium levels. Potassium regulation is largely influenced by catecholamines both inside and outside of cells, as well as by insulin. RBC red blood cells and liver cells contain the remaining portion of the entire amount, with muscles containing around 70% of it [21]. The kidneys are

mostly employed by the body to excrete and absorb excess potassium [22]. Muscle weakness, cramping, and arrhythmias can all be brought on by hypokalemia. It can also be brought on by severe potassium loss through digestion or urine, certain drugs, and kidney disease [23]. Treatment options for treating it include addressing underlying medical conditions and increasing potassium intake with supplements and food [24]. Lowering blood potassium elevation can lead to a variety of common symptoms, including increased loss of potassium through the kidneys, expanded sweating, severe burning, and frequent vomiting that can lead to chemical imbalances in the body. Additionally, supplementary symptoms such as weakness, fatigue, uneven heartbeat, pain, and cramps are common [25,26]. Increased blood potassium levels can cause dangerous symptoms including tingling, muscle weakness, and irregular heartbeat. Prescription drugs, nutritional supplements, diabetes, kidney disease, and other illnesses may cause it [27].

1-3-2 Sodium

Sodium is considered a somewhat significant component that is part of the electrolyte composition of the human body. Human blood and the fluids surrounding cells contain the majority of electrolytes, these are dissolved in physiological fluids that have a charge of electricity. For the typical functioning of neurons and muscles, as well as for the body to maintain a balanced fluid composition, sodium is essential [28]. Sodium, the most common cation in the extracellular environment, is present in numerous foods, including pre-packaged food, meat, dairy, eggs, and vegetables, Sodium plays a relevant role in numerous vital mechanisms in the body, including structural membrane function and water balance inside and outside cells, which affects cellular structure and nerve invigoration, and affects muscle function, including muscle contractions and relaxation [29]. For an adult that weighs 70 kilograms, the total amount of sodium in their body is approximately 60 milligrams per kilogram, or

4200, almost 100 g. Around 1680 milligrams of sodium, or 40% of the total body sodium content, is located in bone. The remainder of the sodium is composed of around 2520 mmol in the extracellular and cellular fluids. The composition of the human body's total sodium content, including the bone, is 10% internal sodium and approximately 50% external sodium [30]. For men who are 14 years old or older, a recommended daily intake of 1,500 mg salts is necessary. However, the maximum risk reduction for chronic diseases (CDRR) is 2,300 mg per day, which is the maximum tolerable amount [31].

1-3-3 Chloride

Since the principal ion that is observed exterior of plasma is chloride, maintaining the acid-base balance is dependent on it. Chloride is additionally necessary to regulate the body's water balance [32]. The distribution of essential fluids is profoundly affected by chloride, as this element has an essential role in maintaining the equilibrium of fluids in and out of cells. Additionally, chloride participates in the manufacturing of stomach acid, which is crucial to the digestion of food and the absorption of nutrients like vitamin B12 and other minerals, these nutrients are important for the body [33]. Chloride facilitates the conservation of renal function and is crucial to the elimination of waste products from the liver [34, 35]. Hyperchloremia is the term for a high concentration of chloride ions in the blood, whereas a low concentration is considered an abnormally high amount. Other symptoms include a low chloride content, which can lead to cramping, fatigue, and muscular weakness. These symptoms can be overcome by increasing the chloride content. Elevated levels of chloride in the body are often caused by medication, dehydration, problems with the kidneys, and a lot of consumption of foods that contain chloride. Unusually high concentrations of chloride can lead to an electrolyte imbalance that has a significant negative impact on the health of a person. The symptoms of increased chloride elevation are variable and include nausea, vomiting,

diarrhea, loss of muscle, rapid breathing, confusion, and fatigue. These diagnostics are caused by high chloride levels, which can be attributed to causes like dehydration, kidney disease, thyroid issues, or

other conditions that affect the body's salt balance [36].

2- Methods and Materials

2-1 Materials

<i>Materials</i>	<i>Company</i>
<i>Human/(TestosteroneII)(TES2) ELFA Kit 30 Tests</i>	<i>Vidas / (France)</i>
<i>Human(electrolyte analyze) Na+, K+, Cl- Kit</i>	<i>Jokoh / (Japan)</i>
<i>Human (IRON 2 kit 200 test)</i>	<i>Roche / (Germany)</i>

2-2 Instruments

<i>Instruments</i>	<i>Company</i>
<i>Adjustable- micropipette (100- 1000UL)</i>	<i>Ependorff e (Garmany)</i>
<i>Adjustable micropipette (10-100 UL)</i>	<i>Ependorffe (Garmany)</i>
<i>(100-1000UL) tip</i>	<i>Ependorffe (Garmany)</i>
<i>(10-100UL) tip</i>	<i>Ependorffe (Garmany)</i>
<i>Centrifuge</i>	<i>Hittich (Japan)</i>
<i>Roche Diagnostics Cobas(C-111 instrument)</i>	<i>Roche Diagnostics (Garmany)</i>
<i>(EX-Ds) without auto- sampler instrument</i>	<i>Jokoh (Japan)</i>
<i>Vidas</i>	<i>bio Merieux(France)</i>

2-3 Subjects

Antiserum samples were assigned to the 50 male participants; 25 of the participants were used as controls, and the remaining 25 men, who were treated from June to October of 2023 at the Nada Adhamiya Center (Iskendarona Medical Group) in Baghdad, had low testosterone levels.

Two groups of participants of different ages were created: the younger and the older.

1-Group 1:- The control group has 25 participants who have normal testosterone levels increased or decreased.

1-Group 2: Low testosterone is observed in half of the men.

2-4 samples Collection

After the puncture of the veins, 5 ml of blood was collected and allowed to coagulate, then centrifuged at 4042 g for 15 minutes.

The serum in this research was divided into two parts: the first was stored at a temperature of -20°C until the time of analysis to determine the following: iron, testosterone, potassium (K), sodium (Na), and chlorine (CL).

2-5 Data collections

Each participant gives their consent to be involved, then a questionnaire is employed to gather all of the relevant information, this information includes the following: name, age, weight, residence, marital status, and smoking.

knowledge of:

- 1- Health history, including any current or recent conditions and the types of drugs consumed.
- 2- Take supplements.
- 3- Taking stimulants only for men.

2-6 Testosterone Procedure

Three milliliters of blood were taken and put into a gel tube "Blood Collection Gel and Clot Activator Tube".

To isolate the tube, it was placed in the centrifuge. From the separated sample, $100\mu\text{l}$ of serum was extracted and added. It was placed in a Cuvette measuring device.

It was put into the VIDAS apparatus. After that, we select "Start".

The test result then appears after 40 minutes of waiting.

2-7. Procedure for the Electrolyte Panel (Na, K, Cl)

Three milliliters of blood were obtained and put into the gel tube "Blood Collection Gel and Clot Activator Tube".

The tube was placed in the centrifuge for separation. From the separated sample, $300\mu\text{l}$ of serum was taken out and put into It was placed in a Cuvette measuring device.

It was transported to the Kokoh device. Next, we choose the word INT.

A thin stalk is present when you pull. Selecting the option of MEAS after inserting the needle into the immunizer sample. The result then appears directly.

2-8. The procedure of the Iron Test

A 3 milliliter blood sample was incorporated into the gel tube which is referred to as the Blood Collection Gel and the Clot Activator Tube.

For division, the centrifuge was filled with the bottle. After the sample was isolated, $300\mu\text{l}$ of serum was removed and placed in a Cuvette that measured the device. That was incorporated into the Cobas c1 device. Next, we choose "order" from the menu.

Ensuing, the definition of the test is given, the sample data is included, and the sample is inserted into the device being evaluated. Next, we select the "start" button, and after ten minutes, the results are exhibited.

3-Result

In this research, 20 healthy controls with an average age of 20-73 were studied, and 50 patients with low testosterone levels were included. Their testosterone, iron, potassium, sodium, and chloride were all tested.

The results demonstrated that the concentrations of testosterone were significantly greater ($P \leq 0.01$) in the control concentration.

The outcomes demonstrated that the iron concentrations were significantly less than the controls ($P \leq 0.01$).

Contrasted with the control, the consequences demonstrated that capable was not a significant difference ($P \geq 0.05$) in Potassium.

Contrasted with the control, the consequences showed that capable was not a momentous difference ($P \geq 0.05$) in sodium.

The results indicate that the concentration of chloride was not different from the control group ($P > 0.05$).

3-1. Testosterone levels in ng/ml compared with control

	<i>No.</i>	<i>Mean±SD</i>	<i>P-value</i>
<i>Control</i>	25	5.47±1.52	
<i>Patients Group</i>	25	1.804±0.841	$P\leq 0.01$

3-2 Concentrations of Iron (ng/ml) compared with control

	<i>No.</i>	<i>Mean±SD</i>	<i>P-value</i>
<i>Control</i>	25	102.0±26.2	
Low testosterone group	25	80.5± 22.8	$P\leq 0.01$

3-3. Levels of Potassium(ng/ml) compared with control

	<i>No.</i>	<i>Mean±SD</i>	<i>P-value</i>
<i>Control</i>	25	4.252±0.381	
Low testosterone group	25	4.399±0.297	$P\leq 0.05$

3-4. Sodium (ng/ml) levels in comparison with control

	<i>No.</i>	<i>Mean±SD</i>	<i>P-value</i>
<i>Control</i>	25	139.01±1.71	
Low testosterone group	25	138.88± 3.00	$P\geq 0.05$

3-5 Chloride (ng/ml) levels comparison with control

	<i>No.</i>	<i>Mean±SD</i>	<i>P-value</i>
<i>Control</i>	25	102.20± 2.22	
Low testosterone group	25	102.08± 2.66	$P\geq 0.05$

4- Discussion

The results demonstrated that individuals with low testosterone levels had lower concentrations of hemoglobin and hematocrit. The amount of iron in the body is directly affected by testosterone, this is accomplished by blocking the iron metabolism's primary regulator [37–40] Compared to men in the highest tier of control, men in the undermost quarter of overall and discharged testosterone are inherently more propensity to have been iron deficient [41].

More research demonstrated that nonobservant of the goal, the new research provides forthright subatomic evidence that the potassium channel in the smooth muscle of the vascular system is augmented by testosterone, this repercussion on the excitability of the vascular system's smooth muscle is documented [42]. The results of the study were that between the testosterone dose groups, there were no significant differences in the baseline concentration of chloride or sodium [43].

Conclusion:

Males who have low testosterone levels are more susceptible to anemia, and hypogonadism may also be a contributing factor. Additionally, electrolyte excretion is through a mechanism dependent on androgen receptors.

Conflict of interest: Nil

Funding: NIL

References

- 1- Shea, Jennifer L, Pui-Yuen Wong, and Yu Chen. "Free testosterone: clinical utility and important analytical aspects of measurement." *Advances in clinical chemistry* 63 (2014): 59-84.
- 2- Kushnir, Mark M, Heather A. Nelson, and Kelly Doyle. "Clinical Utility and Analytical Aspects of Direct Measurements of Free Hormones Using Mass Spectrometry-Based Methods." *The Journal of Applied Laboratory Medicine* 7.4 (2022): 945-970.
- 3- Corona, Giovanni, and Mario Maggi. "The role of testosterone in male sexual function." *Reviews in Endocrine and Metabolic Disorders* 23.6 (2022): 1159-1172.
- 4- Wrzosek, Michał, Jakub Woźniak, and Dariusz Włodarek. "The causes of adverse changes of testosterone levels in men." *Expert Review of Endocrinology & Metabolism* 15.5 (2020): 355-362.
- 5- Feige, Peter, et al. "Orienting muscle stem cells for regeneration in homeostasis, aging, and disease." *Cell stem cell* 23.5 (2018): 653-664.
- 6- Wittert, Gary. "The relationship between sleep disorders and testosterone in men." *Asian journal of andrology* 16.2 (2014): 262.
- 7- Lorigo, Margarida, et al. "Vascular pathways of testosterone: clinical implications." *Journal of cardiovascular translational research* 13 (2020): 55-72.
- 8- Li, Lu, Barry R. Zirkin, and Vassilios Papadopoulos. "Leydig cell androgen synthesis." *Encyclopedia of reproduction* 1 (2018): 215-221.
- 9- Cronin, S. J, Woolf, C. J, Weiss, G, &Penninger, J. M. The role of iron regulation in immunometabolism and immune-related disease. *Frontiers in molecular biosciences*, 6,(2019), 116.
- 10- Chen, Ying, et al. "Iron metabolism and its contribution to cancer." *International journal of oncology* 54.4 (2019): 1143-1154.
- 11- Yameny, A. Ferritin as a biomarker of infection in COVID-19 non-hospitalized patients. *Journal of Bioscience and Applied Research*, 2021; 7(1): 23-28. doi: 10.21608/jbaar.2021.172371
- 12- Maladkar, Manish, Srividya Sankar, and Ashok Yadav. "A novel approach for iron deficiency anaemia with liposomal iron: concept to

- clinic." *Journal of Biosciences and Medicines* 8.09 (2020): 27.
- 13- Ballestín, S. S., Campos, M. I. G., Ballestín, J. B., & Bartolomé, M. J. L. Is supplementation with micronutrients still necessary during pregnancy? A review. *Nutrients*, 13(9).(2021).
- 14- Pasricha, S. R, Tye-Din, J, Muckenthaler, M. U, & Swinkels, D. W. Iron deficiency. *The Lancet*, 397(10270), (2021), 233-248.
- 15- Ambati R, Kho LK, Prentice D, Thompson A. Osmotic demyelination syndrome: novel risk factors and proposed pathophysiology. *Intern Med J*. 2023 Jul;53(7):1154-1162.
- 16- Ellison DH, Terker AS, Gamba G. Potassium and its Discontents: New insight, New Treatments. *J Am Soc Nephrol*. 2016 Apr; 27(4): 981-9.
- 17- Yamada, Shinsuke, and Masaaki Inaba. "Potassium metabolism and management in patients with CKD." *Nutrients* 13.6 (2021): 1751.
- 18- Stone, Michael S., Lisa Martyn, and Connie M. Weaver. "Potassium intake, bioavailability, hypertension, and glucose control." *Nutrients* 8.7 (2016): 444.
- 19- Palmer, Biff F., and Deborah J. Clegg. "Physiology and pathophysiology of potassium homeostasis: core curriculum 2019." *American Journal of Kidney Diseases* 74.5 (2019): 682-695.
- 20- Srinivasa, Vinay. "Potassium and Its Disorders." *Fluid and Electrolyte Disorders*. Intech Open, 2019.
- 21- Weaver, Connie M., et al. "What is the evidence base for a potassium requirement?." *Nutrition Today* 53.5 (2018): 184.
- 22- Viera, Anthony J., and Noah Wouk. "Potassium disorders: hypokalemia and hyperkalemia." *American Family Physician* 92.6 (2015): 487-495.
- 23- Marti, Grischa, et al. "Etiology and symptoms of severe hypokalemia in emergency department patients." *European journal of emergency medicine* 21.1 (2014): 46-51.
- 24- Kardalas, Efstratios, et al. "Hypokalemia: a clinical update." *Endocrine connections* 7.4 (2018): R135-R146.
- 25- Sarnowski, Alexander, et al. "Hyperkalemia in chronic kidney disease: links, risks and management." *International Journal of Nephrology and Renovascular Disease* (2022): 215-228.
- 26- McNaull, Peggy, and Adam Suchar. "Fluids, electrolytes, and nutrition." *Gregory's Pediatric Anesthesia* (2020): 226-246.
- 27- Makuch, Marcelina, and Kamila Tuzim. "Hyperkalemia-a review article." *Journal of Education, Health and Sport* 9.7 (2019).
- 28- Ahmed, Nimat Abdelhaleem Ali, et al. "Evaluation of Serum Total Calcium, Mg, Na+ and K+ Levels in Sudanese Women with Preeclampsia in Shendi town, River Nile State, North Sudan." *World Wide Journal of Multidisciplinary Research and Development* 6.1 (2020): 24-9.
- 29- Morris, Alyssa L., and Shamim S. Mohiuddin. "Biochemistry, nutrients." (2020).
- 30- Preuss, Harry G. "Sodium, chloride, and potassium." *Present knowledge in nutrition*. Academic Press, (2020): 467-484.
- 31- Vaudin, Anna, et al. "Sodium and potassium intake, the sodium to potassium ratio, and associated characteristics in older adults, NHANES 2011-2016." *Journal of the Academy of Nutrition and Dietetics* 122.1 (2022): 64-77.
- 32- McCallum, Linsay, Stefanie Lip, and Sandosh Padmanabhan. "The hidden hand of chloride in

- hypertension." *Pflügers Archiv-European Journal of Physiology* 467 (2015): 595-603.
- 33- Nystrom, Erin, and Whitney Bergquist. "Fluids and Electrolytes: Challenges with Short Bowel Syndrome." *Adult Short Bowel Syndrome*. Academic Press, (2019). 27-43.
- 34- Paller, Mark S. "Pathophysiologic mechanisms of acute renal failure." *Mechanisms of injury in renal disease and toxicity*. CRC Press, (2020). 3-13.
- 35- Jahn, Stephan C., et al. "Chloride concentrations in human hepatic cytosol and mitochondria are a function of age." *Biochemical and biophysical research communications* 459.3 (2015): 463-468.
- 36- Nagami, Glenn T. "Hyperchloremia—Why and how." *nefrologia* 36.4 (2016): 347-353.
- 37- Carrero, J. J, et al., Testosterone deficiency is a cause of anaemia and reduced responsiveness to erythropoiesis-stimulating agents in men with chronic kidney disease. *Nephrology Dialysis Transplantation*, 2011. 27(2): p. 709-715.
- 38- Rotter, I, et al., Analysis of the relationship between the blood concentration of several metals, macro-and micronutrients and endocrine disorders associated with male aging. *Environmental geochemistry and health*, 2016. 38(3): p. 749-761.
- 39- Shin, Y.S, et al., The relationship between serum total testosterone and free testosterone levels with serum hemoglobin and hematocrit levels: a study in 1221 men. *The Aging Male*, 2016. 19(4): p. 209-214.
- 40- Waalen, J, et al., Erythropoietin, GDF15, IL6, hepcidin and testosterone levels in a large cohort of elderly individuals with anaemia of known and unknown cause. *European journal of haematology*, 2011. 87(2): p.107-116.
- 41- Ferrucci, L, et al., Low testosterone levels and the risk of anemia in older men and women. *Archives of internal medicine*, 2006. 166(13): p. 1380-1388.
- 42- Kelly DM, Jones TH. Testosterone: a vascular hormone in health and disease. *J Endocrinol* 2013; 217: R47–71.
- 43- Poliwczak AR, Tylińska M, Broncel M, Testosterone therapy improves the heart rate turbulence without effect on NT-proBNP level in men with metabolic syndrome. *Horm Metab Res* 2014; 46:116-9.