http://www.cjmb.org doi 10.34172/cjmb.2022.13

Open Access Review Article

Crescent Journal of Medical and Biological Sciences
Vol. 9, No. 2, April 2022, 72–80
eISSN 2148-9696

Approach to Anorexia in Chronic Kidney Disease from Avicenna's Point of View in Canon of Medicine: A Narrative Review

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Abstract

Objectives: 35%-50% of patients with chronic kidney disease (CKD) suffer from anorexia, reducing the quality of life and increasing morbidity and mortality. Its causes and definitive treatment are not fully known. In this study, Avicenna's management in his medical book "*Canon of Medicine*" was presented to help solve this problem.

Materials and Methods: "Loss of appetite" and its MeSH heading term "anorexia," also "chronic kidney disease," were searched in PubMed, Google Scholar, and UpToDate databases. In Iranian traditional medicine, loss of appetite by "Noghsan-e-shahvat-e-taam", renal weakness by "Zafe-e-kolye", and ascites by "Estesgha" were searched in "*Canon of Medicine*".

Results: According to Avicenna and modern medicine, kidneys play an essential role in normal appetite, and both suggest treatment based on the stage of the disease. Avicenna has described the treatment in 4 principles: lifestyle modification, elimination of waste products accumulated in the body, non-oral therapies, and herbal medicine. He processed food in the diets, which reduces their side effects and improves their digestion, and in the studies conducted, it was in line with the nutritional recommendations of modern medicine.

Conclusions: Given the importance of anorexia and no known causes and treatment, Avicenna's perspective can help solve this problem. He has provided various natural, inexpensive, and accessible solutions that can be the basis for future clinical trials.

Keywords: Anorexia, Chronic kidney disease, Iranian traditional medicine.

Introduction

Anorexia means a reluctance to eat or decrease energy intake, 35%-50% of patients with chronic kidney disease (CKD) suffer from it (1,2). CKD is an irreversible destruction of kidney tissue or dysfunction in the form of albuminuria greater than 30 mg per day or glomerular filtration rate (GFR) below 60 mL/min/m^2 for at least three months (3), its global prevalence is 11%-13% (4). CKD is the 16th cause of death globally, and 1.2 million people worldwide died in 2017 due to it (5). Protein-energy wasting (PEW) syndrome is an essential factor in predicting the mortality of patients with CKD (6). This syndrome decreases the body's energy and protein stores (7). The most cause of PEW is anorexia which reduces the quality of life and increases morbidity and mortality. Despite the high percentage of patients complaining of anorexia and its serious effects on the lives of patients with CKD, its causes are still not fully understood. Hormones such as ghrelin and leptin, uremic toxins, and inflammation are possible causes (1,8,9).

Treatment of anorexia in these patients is nutritional interventions, pharmacological treatments, proper dialysis dose, and treatment of comorbidities such as heart disease, diabetes, depression, and fatigue (10,11). In patients whose oral nutrition does not meet their nutritional needs, nutritional supplements are prescribed orally or non-orally, such as parenterally or enterally (12). Nutritional supplements taken by patients for six months did not affect body mass index (13), and essential oral amino acid supplements did not increase blood amino acid levels and anthropometric body measurements (14). The effect of supplements and pharmacological treatments, including growth hormone, anabolic steroids, anti-inflammatories, appetite stimulants, and exercise, on increasing survival is known. Still, no significant clinical studies have been performed to investigate their effect on mortality and morbidity (12). Until today, no pharmacological treatment has been identified to prevent or treat PEW-induced muscle atrophy (15). In dialysis patients, increasing the intensity of dialysis was ineffective in improving serum albumin and weight after dialysis. It sometimes even had the opposite effect (16). Avicenna

Received 23 August 2020, **Accepted** 12 January 2021, **Available online** 17 May 2021

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Key Messages

- Staging of chronic kidney disease based on clinical symptoms and physical examination,
- Treatment of anorexia as one of the complications of chronic kidney disease with oral and non-oral treatments,
- Use food processing for better effects and fewer side effects.

(980–1037 AD) is a great Iranian physician who is the author of the medical book "*Canon of Medicine*". This book is one of the valuable medical reference books of Iranian traditional medicine and was taught until the seventeenth century (17,18). Avicenna has mentioned progressive anorexia as a sign of kidney dysfunction and has provided various, inexpensive, and natural solutions to this critical, and common problem.

Evidence Acquisition

In this study, we searched the words "chronic kidney disease" and "loss of appetite" and its MeSH heading term "anorexia" in PubMed, Google Scholar, and UpToDate databases. Also, in Iranian traditional medicine, the book "*Canon of Medicine*" was searched using "Noor Digital Library of Medicine". In the book "Canon of Medicine", Avicenna has described the signs and symptoms of the disease of each organ in detail and has offered various available medicinal and non-pharmacological solutions for treatment. In this study, in the gastric diseases section, loss of appetite or anorexia was searched by "Noghsan-e-shahvat-e-taam", in the section of kidney diseases, the initial stage of CKD was studied as renal weakness by "Zafe-e-kolye" and the advanced stage and ascites were searched by "Estesgha" in the section of liver diseases. Management of anorexia by Avicenna was presented at each stage of CKD.

Results

Avicenna categorized CKD based on clinical signs, physical examination, and urine characteristics and mentioned the management of anorexia at each stage. In this study, the regulation of energy intake and the management of anorexia in CKD are compared from Avicenna's perspective and current studies.

Regulation of Energy Intake in Modern Medicine

The hypothalamus regulates energy consumption; it receives signals from the peripheral parts of the body and regulates energy intake through two groups of neurons. The first group secretes proopiomelanocortin, which increases appetite and catabolism after converting to the melanocyte-stimulating hormone, increases appetite and catabolism, and the second group with Agouti-related peptide and Neuropeptide-Y secretion reduces appetite (1). Eating is influenced by physiological factors such as hunger and sensory stimuli such as olfactory and visual stimuli (19). Ghrelin is a hormone known as the hunger hormone, most of it is secreted by stomach cells, and less is secreted by the intestines, pancreas, brain, and lungs. During fasting, ghrelin is released. After acylation, it stimulates the appetite and increases growth hormone secretion and fat storage in the body; blood ghrelin level returns to normal after a meal (20,21). In addition to appetite, ghrelin also affects sleep, memory, and depression (22). During fasting, another hormone called motilin is secreted from the duodenum and jejunum endocrine cells every 1.5 to 2 hours when the duodenum is acidified, which causes peristaltic solid contractions from the antrum of the stomach and undigested material and bacteria push to the colon. The cholinergic pathway has demonstrated the association of these gastric contractions with motilin and the onset of eating, and the hunger signal. Motilin is known as the "intestinal housekeeper" (20,23,24). When satiated, the leptin hormone, which has anti-ghrelin effects, is secreted from adipose tissue. It reaches the hypothalamus through the bloodstream and inhibits appetite-related neurons, and hormones include Proopiomelanocortin and cocaine amphetamine-regulated transcript (25).

Approach to Anorexia in Chronic Kidney Disease in Modern Medicine

Anorexia means a reluctance to eat. Its cause in CKD is not fully understood, hormonal disorders of leptin, ghrelin, and insulin, inflammatory mediators such as tumor necrosis factor-alpha, neuropeptide Y, melanocyte-stimulating hormone, interleukin 6, uremic toxins, and changes in the level of cannabinoid or cannabinoid-like derivatives in the body are possible causes (1,26). Since the ghrelin is metabolized and excreted in the kidneys (27), in CKD, total ghrelin is increased. Still, only 10% of it is acylated ghrelin, and the rest is unacylated ghrelin, which reduces appetite (28). In CKD, leptin level also increases because the kidneys are the main site of leptin excretion. Leptin causes appetite loss and more energy expenditure, which plays an important role in uremic cachexia (29). Cashexia is the advanced stage of PEW (6). It is a Greek word and consists of two words, "Kakos" meaning "bad", and "hexis" indicating "condition" (30). Today, its symptoms include involuntary weight loss of more than 5% in one year, which is accompanied by three of the following conditions:

1. Anorexia;
2. Fatigue;
3. Weakening of muscle force;
4. Low fat-free mass index;
5. Biochemical changes in the blood include anemia, hypoalbuminemia, and inflammation (31).

Treatment of anorexia in these patients is nutritional interventions, pharmacological treatments, proper dialysis dose, and treatment of comorbidities such as heart disease, diabetes, depression, and fatigue (10,11).

Nutritional interventions are planned according to the stage of the disease. Staging of the disease is done according to the amount of albumin excreted in the urine and GFR and underlying disease. Nutritional programs generally include protein, fat, sodium, potassium, minerals, and vitamins (7). Treatment with nutritional supplements is recommended if serum albumin below 3.8 g/dL or 5% unexplained weight loss within three months (32). For patients who continue to lose weight despite taking the supplement orally or albumin is less than 3.2 g/dL, non-oral nutrition is recommended during dialysis (33); however, in studies, its effectiveness has been the same as oral supplements (32). The effect of supplements and pharmacological treatments, including growth hormone, anabolic steroids, anti-inflammatories, appetite stimulants, and exercise, on increasing survival is known, but no major clinical studies have been performed to investigate their effect on mortality and morbidity (12).

Regulation of Energy Intake in Avicenna's View

In a time of hunger, an appetite stimulant called "Soda" stimulates the nervous tissue of the cardia of the stomach; according to the specifications mentioned in the Canon of Medicine, soda seems to be acidic and is secreted from the pancreas (34,35). Stomach stimulation is transmitted to the brain through the cerebral nerve. At the same time, contractions are created in the stomach's muscle tissue, move the remaining material in the stomach, and prepare the conditions for accepting food. Avicenna mentioned the regulation of energy intake in relation to conditions that include the following:

1. Health of organs such as pancreas, brain, stomach, liver, kidneys
2. Absence of chronic diseases, fever, severe dysentery, parasitic diseases, psychological diseases (sorrow and grief)
3. Favorable taste and smell of food
4. Proper lifestyle such as getting enough sleep and not being in very cold or hot weather and excessive drinking (35).

Approach to Anorexia in Chronic Kidney Disease in Avicenna's View

From Avicenna's point of view, disruption in any part of regulating the energy intake pathway can lead to anorexia. According to Avicenna, the kidneys play an essential role in normal appetite, and progressive anorexia is one of the symptoms of kidney disease, waste that is not excreted due to kidney dysfunction is distributed throughout the body; for example, in the digestive system, it prevents the feeling of hunger by the nervous tissue of the stomach and causes nausea and taste changes that they are among the causes of anorexia. In the Canon of medicine, CKD refers to prolonged kidney disease that leads to impaired kidney function in the excretion of water and waste products. Avicenna categorized CKD based on clinical signs, physical examination, and patient's urine characteristics and described the management of anorexia at each stage.

The Staging of Chronic Kidney Disease in Avicenna's View

First Stage: Avicenna explained various kidney diseases, including diabetes (Ziabitus in Canon of Medicine), congenital kidney diseases, obstructive diseases of the urinary tract such as kidney stones, inflammatory diseases, infectious diseases, and vascular diseases the kidneys. Diseases, if left untreated, can eventually lead to attenuation of the texture of kidney tissue which Avicenna mentioned as "Tahalhol-e-Nasj" or kidney slimming, which Avicenna mentioned as "Hozal-e-Kolye". In this stage, normal function of the kidneys is impaired, and water and waste products gradually accumulate in the body. This stage is called "Zaf-e-Kolye". In new studies, "Hozal-e-Kolye" is considered equivalent to tubular atrophy (11,35).

Second Stage: At this stage, on the one hand, anorexia is due to the accumulation of waste products, and on the other hand, the excretion of substances needed by the body, including proteins through urine, reduces lean body mass. This stage is called "Su-ol-Ghonye" which is composed of two words, "Su" meaning "bad" and "Ghonye" meaning "capital" and in general, it means losing the main capital of the body and losing weight. Symptoms of the "Su-ol-Ghonye" stage are similar to kidney cachexia (Table 1).

Third Stage: Generalized edema and fluid accumulation in the abdomen. This stage is called "Estesgha"(35). The signs, symptoms, and treatments at each stage were listed in Table 2.

Discussion

From Avicenna's point of view, the pathway of energy intake regulation is similar to modern medicine. He has described the signals sent from the stomach to the brain and the contractions of the stomach at the onset of hunger and considered the brain, stomach, kidneys, liver, pancreas to be essential organs involved in normal appetite. In anorexia of patients with CKD, Avicenna also performed treatment similar to modern medicine based on the staging

Table 1. Comparison of Renal Cachexia and Su-ol-Ghonye

Signs and Symptoms of Kidney Cachexia	Reference	Signs and Symptoms of Su-ol-Ghonye	Reference
Anorexia	(31)	Anorexia	(35)
Fatigue		Fatigue	
Decreased muscle mass and low fat-free mass index		Slimming the whole body	
Anemia, hypoalbuminemia, inflammation		White or yellow skin color, edema	

Table 1. Continued

Treatment			Signs and symptoms	Staging	
Foods	Medicines				
	Nonorally	Orally			
• Savigh[a] • Gharis[b] • Masus[c] • Romanieh[d] • Cow's milk, especially with Tarangabin (36)	• Enema with lamb, chicken, cooked animal heads, almond oil, and pistachio oil and dried unripe dates, quince, camel milk and sheep milk	•Hawthorn • dried unripe dates • Sour juices (such as Bergamot, Cherries Sumac, Barberry) with Arabic gum • Flavored vinegar with coriander[e]	• Anorexia • No pain or mild pain in the flanks • Oliguria • Discoloration of urine similar to washed raw meat • Bubble in the urine*	Attenuation of texture "Tahalhol-e-Nasj"	
• Cow's milk, especially with Tarangabin •kidney animal with fragrant spices such as cinnamon and saffron	• Enema with lamb, chicken, cooked animal heads, almond oil, and pistachio oil and dried unripe dates • Poultice with quince, dried unripe dates and damask rose on liver and stomach area on the surface of the skin	• Cinnamon • Saffron • Mastic gum • Clove • Almond • Hazelnut • Coconut • Pistachio • Poppy and beans with sugar	• Anorexia • Slimming the whole body • Mild pain in the flanks white urine • Polyuria • Impotency • Visual loss	Kidney slimming " Hozal-e-Kolye"	**Stage1** (Renal weakness) "Zaf-e-Kolye"
•Zirba[f] •Masus	Poultice with valerian, afsantin, nettle, cinnamon on liver and stomach area on the surface of the skin	• Aloe Vera, • Bisfayej • Cinnamon • Mastic gum •Saffron • Clove • Basil • Lily • Valerian • Nettle • Daikon soaked in oxymel (as an emetic) •Afsantin • Camel milk • Almond oil • Pistachio oil • Sweet Pomegranate • Quince	• Anorexia • Fatigue • Skin discoloration to yellow or white • Edema of the eyelids, face, and limbs • Change in defecation • Sleep disorders • Oliguria • Decreased sweating • Increased bloating • Hydrocele • Inflammation and itching of the gums • Delay in wound healing • Sometimes water accumulates in the lungs	Stage 2 (Kidney cachexia) Su-ol-Ghonye	
•Poultry •Camel milk	• Enema with Iris and *Ferula assa*, foetida gum • Poultice with Frankincense powder and beef fat or figs cooked in water or Saffron, Afsantin and mastic gum with chamomile oil	• Clove • Oregano • Squill • Dill • Cumin • Valerian • Fenugreek • Saffron • Carrot • Lovage • Cardamom • Capparis • Lily root • Damask rose • Anise • Celery • Terminalia chebula • Chicory • Barberry • Nettle • Leek • Ferula assa foetida gum • Almond oil • Pistachio oil • Sweet Pomegranate	• Anorexia • Skin discoloration (sometimes darkening) • Generalized edema and ascites • Thirst • Dyspnea • Boils containing the yellow substance on the skin • Decreased urine • Low-grade fever	Stage 3 (Ascites) Estesgha	

[a] Savigh: Flour made from roasted whole wheat; [b] Masus: Kebab from meat that has been soaked in vinegar first; [c] Gharis: Food made from boiled poultry and cherries; [d] Romanieh: Food made from boiled meat, sour pomegranate, goat fat, and raisins; [e] Aromatic vinegar with coriander: similar to today's coriander vinaigrette sauce; [f] Zirba: The food is first fried dried coriander and onion in almond oil and then cooked with meat of birds such as partridge with a little cumin, vinegar and water, and saffron cloves of mastic and cinnamon are added to it (37, 38).* Today, a bubble in urine can be a sign of proteinuria (39).

of the disease. Today, staging is based on glomerular filtration and albuminuria and the cause of disease, mostly laboratory-based. Still, the staging performed by Avicenna was based on the clinical manifestations, physical examination, and urine characteristics. In general, treatment today includes nutritional interventions and lifestyle modification, pharmacological therapies, and finally, replacement therapy with proper dialysis dose and treatment of comorbidities such as heart disease, diabetes, depression, and fatigue (10, 11). According to Avicenna, treatment includes lifestyle modification, eliminating water, and waste products from the body, oral and non-oral treatments, and herbal medicines. In the nutritional recommendations of modern medicine, regulation of protein consumption, attention to comorbidities such as heart disease and diabetes, and avoidance of allergens play an important role. Avicenna also considered nutritional advice in these patients to be very important in improving lifestyle and prescribed diets. He advised eating less at one meal and increasing the number of meals. He used two food processing methods and added suitable spices and fruits to foods and beverages for better digestion, fewer side effects, and better taste and smell of food. In today's guidelines, protein intake should be adjusted to prevent malnutrition and increase uremic toxins (11). Avicenna emphasized the use of nuts such as Almond, Pistachio, and Hazelnut in these patients (35). Nuts are high in protein (40)، due to the lack of phytase enzyme in humans, phosphate produced from the plant-derived proteins such as nuts are less absorbed than phosphate produced from animal-derived proteins. Today, the use of plant-derived proteins in these patients is recommended (41). Avicenna also recommended the consumption of sour cherry and sumac at the same time if he prescribed animal protein (35).

In today's studies, both prevent an increase in blood uric acid (42,43). Therefore, while providing the protein needed by these patients, the increase of uric acid and phosphate, which are part of uremic toxins, has been prevented. In today's dietary recommendations, controlling diabetes, preventing heart disease, and control blood pressure with low-fat consumption, especially saturated fats and low sodium (11). Some of Avicenna's nutritional recommendations in these patients include the use of nuts, Almond oil, Pistachio oil, unripe Olive oil, Mastic gum, Dill, Basil, Whey, Honey syrup, fish, and adding Arabic gum to juices (35). In addition to having high amounts of unsaturated fats, nuts also contain vitamins and minerals fiber phytosterols, and antioxidant phenols. Consumption of nuts is helpful in preventing cardiovascular disease and diabetes (40). Peptides with angiotensin-converting enzyme inhibitory effects are released during the Almond digestion process (44), drugs in this category today have an influential role in reducing mortality in CKD (45). In today's studies, Almond oil is high in unsaturated fatty acids and has effectively prevented high blood sugar after meals (46). Pistachio kernel oil is high in monounsaturated fatty acids such as oleic, linoleic, and Linolenic acids, which is effective in reducing cholesterol, triglyceride, low-density lipoprotein, and glycemic index (47). Unripe olive oil has richer phenolic compounds such as Oleuropein than ripe olive oil (48). These phenolic compounds have anti-inflammatory, immunomodulatory, antioxidant effects and effectively treat diabetes, heart disease, cancer, viral and bacterial infections, and neurodegenerative brain disorders (49). Olive oil is effective in treating constipation. Fish is a rich source of omega-3, has protective effects on the heart and kidneys, improves lipid profile, and reduces inflammation (50). Arabic gum in modern studies has been effective in reducing fasting glucose and glucose tolerance and improving lipid profile in metabolic syndrome (51).

Mastic gum has strong antimicrobial, anti-inflammatory, antioxidant, anti-diabetic, hepatoprotective, and cardioprotective effects (52). Dill has antioxidant effects and today has a proven role in lowering blood sugar and improving lipid profile (53). Whey protein has all the essential amino acids and has insulinotropic effects, and it is effective in better emptying the stomach (54). Honey syrup is prepared by gently heating a water and honey mixture (35). Recent studies have shown that heating honey destroys the diastase enzyme, converting honey oligosaccharides and polysaccharides to monosaccharides (55). Oligosaccharides and polysaccharides have a lower glycemic index than monosaccharides. Low glycemic index diets are more effective in controlling postprandial blood sugar (56). Honey has antioxidant effects, increases insulin sensitivity, and lowers blood sugar, triglyceride, cholesterol, and low-density lipoprotein (57). The antioxidant activity of honey rises with increasing temperature up to 70 degrees (58). Heat also stimulates immunity through the secretion of granulocyte colony-stimulating factors in-vivo and in-vitro. This effect is not present in honey that has not been heated (59).

Another important dietary recommendation for these patients is to avoid food allergens such as gluten (11). A gluten-free diet that reduces proteinuria in patients with IgA nephropathy has had good effects (60). IgA nephropathy is the most common cause of primary glomerulonephritis, and macroscopic hematuria is one of its symptoms (61). Avicenna likens the discoloration of urine in the first stage of CKD to the color of raw meat washed in water. At this stage, he recommended that the flour consumed by these patients be prepared from roasted whole wheat, and to prepare the bread of these patients, they should mix it with chickpea flour (35). It is now known that roasting wheat before grinding reduces the formation of gluten networks (62). It should be noted that Almonds contain allergenic compounds, and this issue should be considered before consumption (11).

Before grilling meat, Avicenna recommended soaking meat in vinegar and also recommended consuming milk

with Tarangabin (Tarangabin is the manna which is obtained from Alhagi species (36)), and adding Cumin to some foods, and emphasizing the consumption of fruit juices (35). Studies show that soaking meat in vinegar improves the taste and digestion of meat and prevents the production of polycyclic aromatic hydrocarbons, which are carcinogenic and are formed during grilling (63). In one study, the consumption of camel milk with Tarangabin had an influential role in increasing GFR (36). Consumption of juices and Cumin is also appetizing and reduces leptin levels (64). It should be noted that Avicenna forbade the consumption of certain foods, avoiding foods such as legumes in the ascetic stage and sticky foods such as wheat bread without bran. Based on the above, Avicenna's practical and available nutritional recommendations have been in line with modern medicine and considered the prevention and treatment of heart disease, diabetes, metabolic syndrome, depression, and taste and smell changes. In lifestyle modification and nutritional advice, Avicenna also emphasized avoiding overuse of diuretics, insomnia, stress, hyper-sexuality, strenuous activities such as walking or standing for a long time, and equestrian in one is not accustomed to it.

According to Avicenna, the second principle of treatment after lifestyle modification is eliminating water and waste products from the body (35). Nowadays, uremic toxins and excess body fluids are eliminated from the body by pharmacological treatments, dialysis, and finally, kidney transplantation (65). Avicenna has done this in various ways, such as water restriction and causing sweating, vomiting, diarrhea, urination, and finally ascites fluid paracentesis, taking into account the patient's tolerance. To create sweating, he recommended sitting in the sun in a place where there is no wind (35). There are an average of 2.03 sweat glands in a human being that can secrete an average of 1.4 liters per hour when exercising in hot weather. At the time of sweating with water, ions such as sodium and chloride are transported to the skin's surface through the sweat ducts. Still, in the meantime, some sodium and chloride are reabsorbed, and sweat on the skin surface has less osmolality than plasma, so intracellular and extracellular osmolality increase, which reduces ascites fluid (18). Avicenna used Aloe vera as a laxative in these patients (35). In recent studies, the intestinal kidney axis plays a role in intestinal dysbiosis and the worsening of CKD. Also, treating constipation prevents CKD from getting worse (66). The laxative effects of Aloe vera are due to compounds such as emodin and aloin. Aloe vera contains a mucopolysaccharide called Acemannan, one of the most potent immunomodulators, activates macrophages, and has lethal effects on fungi, viruses, and bacteria. It also prevents toxins from passing through the intestines into the systemic bloodstream and helps to regenerate normal intestinal bacteria. This mucopolysaccharide is made in humans until puberty but decreases for reasons such as stress. Aloe vera also has antioxidant, hepatoprotective, and anti-diabetic effects (67) and improves fasting blood sugar, glucose tolerance, and cholesterol (51). The diuretics used by Avicenna include the Ajotva seeds, Fennel, Celery, Anise, Carrot, Valerian, Cloves, Saffron, and Mastic gum (35), most of which have been proven to have diuretic effects today (68). Avicenna has mentioned paracentesis as a last resort and has recommended paracentesis multiple times and low volume each time because he believed that these patients have difficulty healing wounds at the paracentesis site and if a large volume of ascites is removed at once, the patient becomes weak.

Avicenna's third therapeutic principle is non-oral treatments such as enema in patients who cannot eat due to anorexia, taste and smell changes, or depression. He used foodstuffs such as almond and pistachio oils, animal proteins, and fruits such as Quince and unripe, dried Date. There were not many studies in this field. In a study in China in 2017, an increase in blood pre-albumin was reported through enema with plant seeds (69). A poultice is also a non-oral method that has used unripe, dried Date, Valerian, Frankincense powder, and beef fat, and Savigh placed it on kidney, liver, and stomach areas on the surface of the skin. The fourth principle of treatment is the prescription of herbal medicine. It has been used as a tonic for kidneys, stomach, heart, and liver. These plants are Afsantin, Cinnamon, Saffron, fruits such as Pomegranate and Quince.

Today, hepatoprotective, antimicrobial, antioxidant activities, and antiparasitic effects of Afsantin, have been identified (70). Cinnamon is effective in reducing C-reactive protein (CRP), especially in chronic diseases (71). Saffron is an anti-depressant (72) and has effectively controlling metabolic syndrome (73).In new studies, Quince has pharmacological effects such as anti-inflammatory, anti-depressant, diuretic and anti-bacterial and is effective in hepatitis and urinary tract infections (74). Pomegranate fruit also has strong anti-free radical effects, anti-inflammatory and antibacterial activities. Pomegranate has played a nephroprotective role in animal studies by reducing oxidative stress when taking nephrotoxic drugs such as gentamicin (75). It should be noted that Avicenna, in all stages of treatment, has emphasized the patient's condition and tolerance of treatment. For example, laxatives and ascites paracentesis were prohibited in patients with weakness. He also paid attention to the side effects of medicinal plants in these patients. For example, in the event of a fever, it was forbidden to prescribe *Solanum nigrum*, *Cardamom*, and Celery juice. The use of Aloe vera alone is not allowed in the ascetic stage, milk was not prescribed to patients who had diarrhea with milk, he also banned barberry in patients with constipation, and in current studies, barberry has been helpful in the treatment of patients with diarrhea-predominant irritable bowel syndrome (76). According to the above, Avicenna has staged CKDs and treated

them according to each stage, his actions in the field of processing and prescribing appropriate foods together, in addition to providing the protein and calories needed by the body, also prevents the increase of uremic toxins and can play an effective role in controlling comorbidities, such as diabetes, cardiovascular disease and depression also, much herbal medicine used by Avicenna in today's studies have antioxidant and hepatonephroprotective effects and can be effective in preventing the progression of the disease, and he emphasized the use of fragrant and appetizing herbs in patients' diets. Non-invasive methods such as sweating, using an enema to cleanse the intestines and deliver nutrients to the patient through the intestines, and the use of herbal medicine in the form of poultices in these patients can be the basis of future studies.

Conclusions

In this study, it was found that Avicenna mentioned the staging of CKD with precise signs and symptoms and offered various treatments and food processing. Food processing causes better digestion and taste and reduced side effects, many of which are similar to today's nutrition guidelines. Due to the 35-50% prevalence of anorexia in CKD and the burden of global health, using the Avicenna approach can help solve this problem.

Authors' Contribution

MM and SAL designed the study and conducted the research. NS, MK, AAH, MS monitored, evaluated, and analyzed the result of the study. Further, MM and SAL reviewed the article. All authors approved the final manuscript and took responsibility for the integrity of the data.

Conflict of Interests

The authors declare no conflict of interest.

Ethical Issues

The present study was approved by the ethics committee of Arak University of Medical Sciences, Arak, Iran (Code: IR.ARAKMU.REC.1398.288).

Financial Support

None to be declared.

Acknowledgments

This review was extracted from the Ph.D. thesis of the Complementary Medicine Research Center of Arak University of Medical Sciences. The authors would like to thank Arak University of Medical Sciences for their support.

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