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Review

Chronic Kidney Disease and Its Comparison with Hozal-e-Kolye in Persian Medicine

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Abstract

Chronic kidney disease (CKD) is recognized as a major global health problem, which is associated with numerous complications. This disease is characterized by kidney dysfunction and a reduced glomerular filtration rate. Among the main causes of this disease, we can refer to hypertension, diabetes, autoimmune diseases, and polycystic kidney disease. Despite the recent treatments, we are witnessing a rise in the cases of disease progression and the need for renal replacement therapy. The present study aimed to assess the causes and symptoms, as well as prevention and treatment options for Hozal-e-Kolye (kidney atrophy) in Persian medical texts and compare it with CKD. To conduct this study, the terms related to "Hozal-e-Kolye" were searched in reliable and available books of Persian medicine such as Al-Qanoon fi al-Tibb, Sharh-ol-asbab va al alamat, Zakhire -e kharazmshahi, Teb-e-Akbari and other resources. To examine the CKD, all reliable medical books, such as Harrison and Brenner, as well as PubMed, Science direct, and Scopus databases were used. Following that, a comparison was made between the extracted data on Hozal-e-Kolye and those about CKD. According to the results of this study, common points were seen between the causes and symptoms of Hozal-e-Kolye and chronic kidney disease. In Persian medicine, the treatment of Hozal-e-Kolye includes removing the causes of the disease, and then performing treatments to hydrate kidneys. These treatments can be used in CKD patients, based on the similarities between these two diseases. Considering the similarities in the causes and symptoms of Hozal-e-Kolye and CKD, these two diseases can be deemed close in nature, and accordingly, research ideas can be designed and implemented to prevent and help treat CKD.

Keywords: Chronic kidney disease; Hozal-e-Kolye; Persian medicine

Introduction

Chronic kidney disease (CKD) is a major global health problem [1] with a rising incidence, poor prognosis, and high cost [2]. This disease is characterized by kidney dysfunction and a reduced glomerular filtration rate. Among the main causes of this disease, we can refer to hypertension, diabetes, autoimmune diseases, and polycystic kidney disease [3]. Cardiovascular problems, serum lipid disorders, bone disorders, electrolyte disorders, anemia, malnutrition, and metabolic acidosis are the critical complications of this disease [4].

Two major mechanisms participate in the pathophysiology of CKD: specific initiating mechanisms for underlying causes (genetic disorders in kidney development, deposition of immune complexes and in-

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flammation in some types of glomerulonephritis, exposure to toxins in some diseases of renal tubules and interstitial tissue) and non-specific mechanisms which include hyperfiltration and hypertrophy of remaining nephrons, caused by chronic reduction in renal mass. The decrease in the number of nephrons results in the response of vasoactive hormones, cytokines and growth factors that eventually results in disintegrating of glomerular structure, leading to abnormal podocyte function and disruption of the filtration barrier which is due to increasing pressure and flow. This procedure ends in sclerosis and destruction of the remaining nephrons, resulting in severe decrease in kidney function [3]. In the pathological study, there is advanced glomerular scar and sometimes complete sclerosis. Interstitial fibrosis associated with atrophy and dropout of many of the tubules in the cortex and reduction of the capillary network around tubules can also be seen. The small and medium-sized arteries are often thick-walled with narrowed lumina, secondary to hypertension. There is lymphocytic infiltration in the fibrotic interstitial tissue [5]. In renal ultrasound, bilateral smallness of the kidneys with irreversible scars can be seen [3].

In classical medicine, common treatments, including drug treatment and diet, are performed in the early stages of CKD to reduce the speed of disease progression [3].

With the progression of the disease, kidney function decreases and the accumulation of uremic toxins leads to adverse biological effects [6], such as uremic syndrome. At this stage, the patient needs dialysis and kidney transplantation to survive [3].

Despite the remarkable treatments and efforts, we are witnessing a sharp rise in the cases of disease progression and the need for kidney transplantation [7].

Today, the use of traditional and complementary medicine has increased significantly around the world; as a result, in the last three decades, the World Health Organization has emphasized the revival of traditional and complementary medicine in different regions of the world [8].

Persian medicine is one of the most distinguished and oldest medical schools that has made a great contribution to the history of medicine [9]. "Hozal-e-Kolye" has been mentioned in reliable resources of Persian medicine that seems to be related to CKD.

The importance of the disease, its high prevalence, its adverse effects on patients' quality of life, its economic burden, and the inadequacy of existing interventions have made the use of traditional and complementary medicine capacities in the field of prevention methods and safe and effective treatments an undeniable necessity.

In light of the aforementioned issues, the present study aimed to elucidate Hozal-e-Kolye, identify its causes, symptoms, and treatments in Persian medicine, and compare it with CKD in modern medicine.

Materials and Methods

To carry out this study, reliable and available books of Persian medicine such as Hedayat-o al-motaallemin, Al-Qanoon fi al-Tibb, Sharh-ol-asbab va al alamat, Zakhire -e kharazmshahi, Teb-e-Akbari, Exir-e-Azam and other resources in the software of the comprehensive library of medicine (version 1.5) were reviewed and the terms "Laghari-e Kolye", " Laghari-e Gorde", "Hozal-e-Kolye" and "Hozal-e- Gorde" which came under kidney diseases, were searched and collected.

The extracted data were placed under the headings of definition, causes, symptoms, and treatment, and common and disputed points among different resources were categorized and analyzed.

Furthermore, to investigate CKD, the authoritative medical books of Harrison and Brenner, as well as PubMed, Science direct, and Scopus databases, were searched using the keywords: "Chronic kidney disease" and "Chronic renal failure", as well as the combination of these two keywords with Symptom, Complication, and Treatment. Thereafter, the extracted data of Hozal-e-Kolye and CKD were compared and the results were presented through tables and text.

Results

Hozal-e-Kolye

A) Kidney anatomy in Persian medicine

The kidney is semicircular and has dense and hard tissue, the convex part of which is towards the dorsal vertebra [10].

The kidney includes kidney tissue, fat, and blood vessels and lacks sensation by itself; however, the surrounding membrane has a lot of sensation [11].

Kidneys are connected to the posterior abdominal wall by strong ligaments. The vena cava comes from the liver to the kidney and branches into two blood vessels. One of the branches is for blood supply and nutrition of the kidney tissue, and the other branch absorbs the liquid in the blood, which is urine. Both kidneys are connected to the bladder, and blood and urine travel through the kidneys to the bladder [12].

B) Definition of Hozal-e-Kolye

Hozal means thinness and the loss of muscle mass and fat [13], and therefore, Hozal-e-Kolye in Persian medical resources also means kidney shrinkage [10,11,14-16].

Avicenna, in the definition of this disease, in addition to shrinkage, mentioned the reduction or loss of kidney fat, which has also been pointed out in several other resources [17-19]. However, in addition to kidney fat reduction, Kermani has referred to the loss of

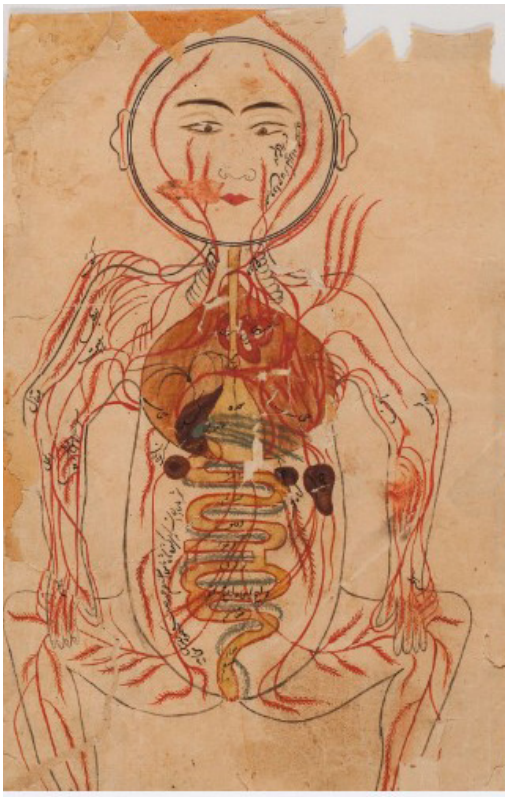

Figure 1. Position of the kidneys in the book of "Tashrih-ol-abdan"

kidney tissue [19]. In another book, Heravi has only mentioned the reduction or loss of kidney tissue in the definition of this disease [20].
Based on this, Hozal-e-Kolye can be defined as kidney shrinkage due to the reduction or loss of kidney fat and tissue.

C) Causes of Hozal-e-Kolye
In the resources of Persian medicine, 3 general causes have been mentioned for Hozal-e-Kolye:
1. Dystemperament that includes warm, cold, and dry dystemperaments; nevertheless, most of the resources have considered warm dystemperament to be involved in causing Hozal-e-Kolye [10,11,16,18,19,21-24].
In Persian medicine, it is believed that each part of the body organs include a certain amount of warmness, coldness, dryness, and wetness qualities, which is called temperament. As long as the organs of the body are moderate on their own temperaments, they will have a normal function; however, if they deviate from their normal temperament, a process will begin that will eventually lead to a disease or so-called dystemperament, in which the function of the organ will be disturbed [25].
2. Frequent and excessive excretion of material (Estefraghat): one of the treatment methods in Persian medicine is to remove the disease-causing substance or waste materials from the body. This method is called Estefragh, such as phlebotomy (Fasd), cupping therapy (Hejamat), Leech therapy, laxatives and diuretics. One of the important causes of Hozal-e-Kolye is excessive excretion of material , such as excessive consumption of laxatives and diuretics and excessive blood loss [10,11,16-19,21-23].
3. Excessive sexual intercourse: this cause is one of the methods of removing substances from the body; nonetheless, due to its great importance, it is mentioned in an independent chapter in most resources [10,11,16-19,21-23]. Excessive sexual intercourse causes extreme heating of the genitals and weakness of the kidney tissue, and due to the depletion of kidney tissue and fat, it causes a decrease in its strength and leads to its weakness [19].
D) Symptoms of Hozal-e-Kolye
The symptoms of this disease can also be divided into two general categories, including general symptoms and specific symptoms.

General symptoms

1. Body thinness [11,15-19,21-24]: the causes of Hozal-e-Kolye can lead to the loss of moisture and tissue disintegration of some organs, which eventually results in the thinness of the whole body. Moreover, due to the physiological partnership with the liver, Hozal-e-Kolye causes liver weakness [21] and the liver becomes unable to digest food and produce humors and organs; as a result, the body becomes thin.
2. Musculoskeletal symptoms: including back pain and coldness of the kidneys [10,11,15-19, 21-24], which are caused due to kidney involvement [21].
3. Headache [10,11,16,18,22]: according to the knowledge of Persian medicine, the kidney participates with the brain through the liver; therefore, if the kidney is affected by a disease, in some cases, the symptoms of this disease also appear in the brain. For example, a headache in Hozal-e-Kolye is due to a disease in the kidney, which participates with the brain in one or more functions. In these types of diseases, which are called participatory diseases (mosharekati), if one organ contracts a disease, its partner organ may contract a disease as well [21,22].
4. Visual impairment [10,18,21,22]: in Persian medicine, one of the causes of visual impairment is kidney weakness and general body weakness [21].

Specific symptoms

1. Urinary symptoms:
a) in the form of increased volume, incontinence, whiteness, and dilution of urine [10,11, 15-19,21-24,26], which due to the weakness of the kidney in absorption, waste materials are not absorbed from the liver and the urine becomes diluted [27].
b) the formation of a cloud of fat in the urine [24]:

in the resources of Persian medicine, a type of white urine called "Dasemi" is mentioned, which is caused by the solving of fat [27].

2. Sexual disorders (decreased libido and impotence) [10,11,15-19,21-24]:

One of the causes of decreased libido in Persian medicine is kidney diseases, including Hozal, and this is due to the role of kidneys in sperm production [11].

E) Prevention and treatment of Hozal-e-Kolye

Important points have been mentioned in Persian medicine for the prevention and treatment of this disease. Preventive measures include avoiding excessive sexual intercourse and excessive consumption of diuretics, laxatives, and foods and medicines with a very warm or very cold and drying (desiccant, Mojaffef) temperaments, as well as excessive bloodletting [11,16,18,19,21]. Based on this, it is possible to prevent this disease by avoiding excessive consumption of salt, which has a warm and dry temperament and acts as a natural desiccant, as well as avoiding any activity that causes excessive dehydration, such as heavy sports with sweating and a dry sauna.

The treatment of Hozal-e-Kolye first includes the removal of the causes of the disease, and then the administration of oral and non-oral treatments. One of the mentioned treatments for Hozal-e-Kolye is fattening measures [11,19]. Patient nutrition has a special place in obesity measures. Among the food treatments with the most emphasis in the resources, we can mention the consumption of nuts, including almonds, pistachios, hazelnuts, and chilgoza pine, with sugar. Eating nuts with sugar is the favorite of the body's nature because of their fat and sweetness; therefore, this combination is in complete harmony with the body nature of the body and produces pleasant blood for the body organs; as a result, the organs absorb them with full enthusiasm and will become obese. This matter applies specifically to the kidney because the kidney has hard and solid tissue, and the blood feeding it should be appropriate for it [19].

Another common treatment is feeding with animal fats and proteins. Nutritional and medicinal treatments for Hozal-e-Kolye are listed in table 1.

Non-oral treatments are in the form of hoqne (enema), poultices, and oil massage. Hoqne is a therapeutic method in which liquid medicine is injected into the intestines through the anus [28]. In the al-Qanun fi al-Tibb, the main ingredients used in the preparation of the hoqne fluid useful for Hozal-e-Kolye include the meat and head of sheep and chicken along with oils, such as nuts and sheep tail fat oil, as well as warm fresh milk [23].

In addition to these, pigeon meat, kidney fat [22], lamb leg [18], and legumes, such as wheat, chickpeas, lentils, beans, and broad beans, have also been mentioned in this regard [11,19].

Local treatments include massaging back with oils, such as violet, almond, pumpkin, and chicken and goose fat [26], and goat kidney fat poultice [18].

Table 1. Nutritional and medicinal treatment of Hozal-e-Kolye in Persian medicine resources

Row	Food category	Example	References
1	Nuts	Almond, hazelnut, coconut, pistachio, chilgoza pine, walnut	[10,11,14-19,21-23,26, 29,30]
2	Animal fat	Schmaltz (chicken, duck, and goose), kidney fat, animal butter	[10,11,14,17-19,21-23, 29]
3	Animal protein	Kidney tissue, fish, khash, fat chicken, lamb, squab, soft-boiled eggs, red beef	[10,11,14-18,21-23,26, 29, 30]
4	Legumes	Chickpeas, beans, broad beans	[21-23,29]
5	Milk and its food products	Cow's and sheep's milk, Rice pudding with sugar, Porridge, Dava al-Taranjabin	[11,15-17,19,21,23,26, 29]
6	Wheat and its products	Hariseh; bread with tallow, ginger, anise, and dry coriander	[10,11,14,16-19,21,22, 26, 30]
7	Fruit	Dates, figs, pears, melons, grapes, raisins, bananas	[15,18,21,30]
8	Materia medica	Pumpkin seeds, cucumber seeds, cotton seeds, Opium poppy, lak, wild pistachio , nutmeg, onion, myrtle, parsnip, carrots, leeks, bindii, sesame, tala, heart of palm, asafoetida, cyperaceae, long pepper, Narmushk, Alyssum, Spruce seed, asparagus, anise, taro	[10,14,17,21-23,29,30]

Discussion

The findings of this research showed that Hozal-e-Kolye (kidney atrophy) and CKD were relatively similar. This similarity can be found in the causes and especially in the symptoms of these two diseases. They may not be similar in other ways; however, they are comparable.

Comparison of the definition of Hozal-e-Kolye and chronic kidney disease

The type and criteria of the definitions of this disease are different in schools of classical medicine and Persian medicine. Based on this, it can be said that Persian medicine's definition of Hozal-e-Kolye is anatomical and refers to the slimming and shrinking of kidney size, while the common medicine definition of CKD is a functional one based on laboratory criteria. Therefore, since these two definitions are different from each other in terms of their criteria and measurement tools, they are not very similar.

From the definition of Hozal-e-Kolye, it can be understood that this disease occurs when the fat inside or around the kidney is reduced and in severe cases, it disappears. One of the benefits of the presence of fat tissue in the body is moisturizing the organs [31]. In this case, with the reduction of the moisture of the kidney tissue and its dryness, it shrinks, which is called Hozal-e-Kolye. Therefore, it can be said that Hozal-e-Kolye means kidney shrinkage as a result of the reduction or loss of kidney fat and tissue.

As mentioned before, in CKD, the decrease in the number of nephrons causes the response of vasoactive hormones, cytokines, and growth factors, and with the increase in pressure and flow, the glomerular structure and the filtration barrier are disturbed, and finally, it causes sclerosis and destruction of the remaining nephrons [3]. Morphologically in CKD, the kidneys are symmetrically contracted and shrunk. Advanced glomerular scar, complete sclerosis, interstitial fibrosis and reduction of the capillary network around the tubules are seen [5].

Comparison of kidney anatomy in Persian and classical medicine

According to Persian medical texts, the kidney includes tissue, fat, and blood vessels [11]. In the resources of classical medicine, the central echogenic structures of the kidney include vessels, calyces, and renal sinus fat, which can be observed in the ultrasound of a normal kidney [32]. Furthermore, right outside the kidney capsule, there is a mass of extraperitoneal fat (perinephric fat) completely surrounding the kidney [33]. Perhaps in Persian medicine "kidney fat" refers to kidney sinus fat and what is said about "fat on the kidney" refers to perinephric fat.

According to resources of Persian medicine, the kidneys are connected to both sides of the back by means of strong ligaments [12]. In the new anatomy, similar to this, it is stated that in the lateral margins of each kidney, the anterior and posterior layers of the renal fascia are connected to each other and are connected to the transversalis fascia in the lateral abdominal wall [33]. Therefore, the ligaments mentioned in Persian medicine can be considered the anterior and posterior layers of the renal fascia, which are connected to the transversalis fascia.

Anatomical changes in chronic kidney disease include bilateral smallness of kidneys with irreversible scars [3]. This smallness of the kidney is also mentioned in Persian medicine.

Comparison of causes of Hozal-e-Kolye and chronic kidney disease

One of the similarities between these two diseases is their causes. One of the causes of Hozal-e-Kolye is excessive bleeding and excessive use of laxatives and diuretics. On the other hand, bleeding and loss of body fluids through digestion (diarrhea) and urine (diuretics), are among causes of Pre-renal azotemia [32]. Pre-renal azotemia is one of the causes of acute renal failure [3] and one of its most common complications is CKD [34].

Comparison of symptoms of Hozal-e-Kolye and chronic kidney disease

Another aspect of the similarity between these two diseases can be found in their clinical symptoms, such as body thinness, sexual disorders, and musculoskeletal pains. Sexual dysfunction is also common in patients with CKD. One of the most prevalent manifestations of sexual dysfunction in men with CKD is erectile dysfunction, and its prevalence is reported between 70% and 80%. Decreased libido and infertility are also common in both genders [35]. More than 65% of women undergoing hemodialysis have reported sexual disorders [36]. Table 2 presents the corresponding symptoms of Hozal-e-Kolye and CKD.

In addition to the mentioned symptoms, in Persian medicine, "bad breath" is also mentioned in most cases of kidney diseases, which can correspond to uremic fetor in the resources of new medicine. It is also mentioned in the resources of Persian medicine that kidney disease can lead to heart, lung, and respiratory diseases [11,21] and this corresponds to shortness of breath and chest pain in patients with CKD [37]. The symptoms of dry skin, dry mouth, feeling sad, irritability, numbness or tingling of the legs, and sleep disorders [37] can be explained by considering the cold and dry dystemperaments in these patients.

According to the above issues, both in Hozal-e-Kolye and in CKD, the amount of moisture in the kidney is reduced (it is dried) and this causes the kidneys to shrink.

Table 2. Corresponding symptoms of Hozal-e-Kolye and chronic kidney disease

Row	Symptoms of Hozal-e-Kolye	Symptoms of chronic kidney disease
1	Body thinness	Protein-energy malnutrition [3] Muscle atrophy [32]
2	Increased urine volume, urinary incontinence	Polyuria, nocturia [6]
3	Formation of a fat cloud in the urine	Foamy urine (due to proteinuria) [3]
4	Decreased libido, impotence	Decreased libido, impotence [37]
5	Back pain	Muscle pain [37], muscle cramps [6], bone pain [3], back and flank pain [32]
6	Headache	Headache [37]
7	Poor eyesight	Diabetic retinopathy [3], retinopathy caused by diabetes and hypertension [32]
8	Renal shrinkage	smallness of both kidneys [3]

Comparison of the treatment of Hozal-e-Kolye and chronic kidney disease

In common medicine, the treatment and prevention of the progression of CKD are through diet and blood pressure control drugs. If the disease progresses and causes renal failure, dialysis and kidney transplant are performed [3]. In Persian medicine, the primary and important treatment for Hozal-e-Kolye is based on removing the causes of the disease. Then, oral and non-oral treatments are administered with the aim of increasing the size of and moisture in the kidneys and removing their dryness.

One of the notable cases in the control of CKD is the restriction of protein intake [38], and according to this point, it is possible to use the proteins mentioned in the resources of Persian medicine within the permissible limit based on the patient's condition. Moreover, one of the advantages of the therapeutic methods of Persian medicine is the use of local treatments, which can also be recommended.

Conclusion

Although the difference in the conceptual foundations between Persian medicine and modern medicine makes it difficult to make a comparison, the similarities in the causes and symptoms of Hozal-e-Kolye with CKD show that these two diseases can be deemed close in nature, and therefore, the effectiveness of the measures and treatments for Hozal-e-Kolye in Persian medicine is predictable to some extent for CKD. In particular, the treatment of Hozal-e-Kolye is based on dietary instructions to a significant extent, which can be considered as an advantage in the treatment process proposed by Persian medicine. Accordingly, it is suggested that descriptive and analytical studies be conducted to prove the relationship between the causes of Hozal-e-Kolye and CKD, and clinical trials need to be designed based on Hozal-e-Kolye treatments for CKD.

Conflict of Interests

None.

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