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# The Cystinuria Cardiovascular Epidemiology

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## Abstract

Mainly, cystinuria is a rare renal stone disease, which individuals inherit from their family members. The genetic disorder is characterized by gene mutations in SLC3A1 and SLC7A9 and encoding proteins that enhance dibasic amino acid exchange expressed in the proximal tubule of the kidney and the gut. Cystinuria affects approximately one in 7,000 persons in the United States. Individuals with cystinuria experience signs and symptoms, including nausea, vomiting, pain while urinating, blood in the urine, and pain near the abdomen or groin. Patients experience blockage of the ureter, urinary tract infections, kidney infections, and bladder or kidney damage because of untreated cystinuria. The study focuses on examing pharmacological and non-pharmacological treatment methods for cystinuria, including Cystine-Binding Thiol Drugs (CBTD), urinary alkalinization, surgical procedures, dietary modification, and hydration. The researcher completed secondary research that focused on online information from governmental reports, academic institutions, journal databases, and credible newspapers and magazines. It utilizes information from peer-reviewed journals, e-books, and government and non-governmental reports published within the last ten years. Although the literature review provides adequate and detailed information on pharmacological and non-pharmacological treatment methods for cystinuria, the articles fail to provide convincing information on accurate dosages of medications for adults and children and the short and long-term side's effects of the treatment methods. Nonetheless, clinicians should apply the knowledge from the peer-reviewed articles in managing and treating cystinuria.

The clinical significance of the literature review, especially the topic is to:

Promote early diagnosis and treatment of cystinuria among adults and children.

Enhance the clinical outcomes of patients with cystinuria.

Reduce the adverse complications and symptoms of cystinuria among Americans.

Improve stakeholders', clinicians and patients, knowledge of managing and treating cystinuria.

**Keywords:** Preventives; Cystinuri; Cystine-Binding Thiol Drugs (CBTD); Urinary alkalinization; Surgical procedures; Dietary modification; Hydration.

## Introduction

Cystinuria is among the prevalent genetic diseases in the United States is a rare renal stone disease, which individuals inherit from their family members [1]. The genetic disorder is characterized by gene mutations in SLC3A1 and SLC7A9 and encoding proteins that enhance dibasic amino acid exchange expressed in the proximal tubule of the kidney and the gut [2]. National Organization for Rare Diseases indicates that cystinuria affects approximately one in 7,000 persons in the United States [2]. It implies that the disease only accounts for roughly 1% to 2% of kidney stones among Americans. Admit that men two times more vulnerable to cystinuria than females [3]. The disease affects children increase their risks of all renal calculi complications by 6% to 8%. Individuals with cystinuria experience signs and symptoms, including nausea, vomiting, pain while urinating, blood in the urine, and pain near the abdomen or groin. Persons with cystinuria begin to experience adverse signs and symptoms of the complication between 10 and 30 years [2]. National Kidney Foundation argues that persons that fail to seek early and adequate treatment for cystinuria suffer from adverse complications, such as the blockage of the ureter, urinary tract infections, kidney infections, and bladder or kidney damage [2]. In this regard, individuals require adequate and evidence-based treatment and prevention methods to overcome cystinuria's adverse symptoms and complications [1-2]. Therefore, the literature review will comprehensively analyze the evidence-based pharmacological and non-pharmacological treatment methods for cystinuria [2].

## Literature Review

### Methods of data collection

The collection of data and information to complete the literature review on the evidence-based pharmacological and non-pharmacological treatment methods for cystinuria is based on secondary research [3]. Secondary research involves using existing data or information to complete studies [3,4]. Secondary research methods entail reviewing and accessing quality data and information from educational institutions,

public libraries, informational resources on the internet, and reports from government and non-government agencies [4]. In this study, the secondary research will focus on online information from governmental reports, academic institutions, journal databases, and credible newspapers and magazines [2]. Specifically, the research will prioritize information from peer-reviewed journals, e-books, and government and non-governmental reports published within the last ten years [1]. The scholar plans to access Google Books to access good e-books with relevant information and data about the topic. Also, the researcher will log in to ProQuest, Google Scholar, and other peer-reviewed databases to access quality and up-to-date journals with relevant information on the selected topic. The researcher plans to utilize key phrases like "evidence-based treatment and management methods for cystinuria,"pharmacological approaches for treating cystinuria," or "non-pharmacological methods for managing and treating cystinuria" to access adequate articles for the literature review. The scholar selected the secondary research methods because it is inexpensive, less time-consuming, and increases access to the readily available information [4]. On the contrary, the method is disadvantageous as the researcher may struggle to access information specific to the study's needs [5].

## Pharmacological management of cystinuria

Physicians use different types of evidence-based medicines in treating cystinuria to increase the solubility of cystine in the urine indicate that clinicians utilize Cystine-Binding Thiol Drugs (CBTD), including D-penicillamine, tiopronin, captopril, and bucillamine. D-penicillamine is among the most effective oral administration of thiol-containing medications for the effective treatment of cystinuria [6]. The medicine combines with urinary cystine to minimize crystallization in the kidney [2]. D-penicillamine dissolves pre-existing stones and reduces the formation of new kidney stones in patients with cystinuria. Most clinicians resort to the use of D-penicillamine when alkanization and hydration fail in the treatment of cystinuria [4-5]. Even though D-penicillamine is effective, the medication's side effects involve a high incidence of dose-limiting toxicity and autoimmune disorders admit that more than 84% of patients that undergo D-penicillamine therapy experience adverse side effects of the medication [3]. Medical practitioners should overlook the side effects of the drug due to its effectiveness in addressing and preventing adverse symptoms of cystinuria. Alternatively, clinicians use tiopronin for managing cystinuria [1-2]. The therapy involves administering oral tiopronin for cysteine dissolution and preventing the reoccurrence of stones in the kidneys of patients with cystinuria. Some researchers conducted a study involving 66 patients to evaluate the effectiveness of tiopronin in treating cystinuria. argue that clinicians gave the patients daily doses of 1,193 mg of tiopronin during their long-term treatment [3]. The medication ensured cystine levels of the patients remained at 350 mg to 560 mg per day and urinary cystine were at unsaturated levels adds that tiopronin reduced stone formation in approximately 94% of the patients [5]. Tiopronin is effective in treating adults and children with cystinuria. Although the medication is effective, it has side effects, including bloating or swelling of the face, abdominal discomfort, unusual weight loss, blurred vision, and irregular heartbeat. Furthermore, clinicians rely on captopril to reduce cystine excretion to inhibit stone formation in patients with cystinuria argue medical practitioners used captopril in treating patients with homozygous cystinuria [4-6]. The medication reduced cystine excretion in one of the patients by 70% after only twenty-six weeks. In the second patient, admit that captopril minimized cystine excretion by approximately 93% after nine weeks [7]. The positive findings of captopril administration proved that it is an effective evidence-based method for treating cystinuria. It essential to note that none of the patients involved in the study showed side effects of the medication [5]. Equally important, medical practitioners use evidence-based urinary alkalinization medications for treating patients with cystinuria. Physicians utilize urinary alkalinization medications to prevent cystine precipitation, stone formation and dissolve existing cystine stones in patients with cystinuria [4-6]. Urinary alkalinization entails using sodium bicarbonate or potassium citrate to increase or maintain urinary pH to a level of 7.0 to 7.5. The rate of cystine solubility is high in patients with a urinary pH of 7.0 to 7.5. Patients need to combine urinary alkalinization with animal protein restriction to overcome the adverse effects of cystinuria [3-5].

## Surgical therapies

Medical practitioners recommend evidence-based surgical methods for treating cystinuria. Clinicians use minimally invasive surgical procedures when pharmacological approaches fail to remove or break up kidney stones [2]. Mainly, doctors perform percutaneous nephrostolithotomy surgery on patients with indicate that percutaneous nephrostolithotomy surgery involves passing a special instrument through patients' skin into their kidneys to break or take out stones, causing cystinuria [4]. The procedure leads to the passage of kidney stones through urine drainage in patients with cystinuria indicate that medical practitioners only use the percutaneous nephrostolithotomy surgical method to manage, break, or take kidney stones larger than 20 mm [6]. Even though the percutaneous nephrostolithotomy surgical procedure is effective, it has a surgical complication rate of around 15.4%. Additionally, clinical facilities utilize ureteroscopy for treating cystinuria ureteroscopy surgical procedure involves passing a tiny instrument into patients' bladder, then into their ureter to drain urine and remove kidney stones [3,4]. Medical practitioners use the ureteroscopy surgical procedure to remove kidney stones between 12 to 20 mm. In a study,indicate that applying a ureteroscopy surgical procedure led to the successful treatment of 71% of patients with cystinuria [1-4]. The treatment method has a high complication rate of roughly 23.8%. Alternatively, medical practitioners use Extracorporeal Shock Wave Lithotripsy (ESWL) for treating patients with cystinuria [4]. The ESWL surgical method allows medical practitioners to use shock waves to break large stones in the kidney into small stones [5]. That clinicians use the ESWL surgical method to remove kidney stones smaller than 12 mm. Although ESWL surgical method is an effective treatment method, its complication rate is around 11.4% [2-3]. Thus, medical practitioners should appropriate

surgical methods for managing or treating patients with cystinuria only after pharmacological methods failure [5].

### Behaviour management approaches

Clinicians and health facilities recommend the application of hydration in managing and treating cystinuria [4]. The hydration method requires patients with cystinuria to maintain a high intake of fluids to produce a minimum of three liters of urine daily [3]. Medical practitioners advise patients with cystinuria to drink plenty of water during the day and at night. For example, physicians encourage patients to take at least 500 mL of water before sleeping and an additional 300 mL overnight [2]. The high intake of water ensures patients keep their urinary cystine levels under 300 mL indicate that maintaining a high water intake and urine output leads to increased cystine excretion, reducing the risk of kidney stone formation also, clinicians and health facilities apply diet modification to manage and treat cystinuria [2-4]. Diet modification is essential as it reduces the risk of stone formation in patients with cystinuria. Moussa, Papatsoris, and Chakra (2020) state that medical practitioners encourage patients to consume low sodium and animal protein foods in diet modification. Food low in sodium increases the reabsorption of cystine, reducing urinary cystine excretion indicate that low intake of animal protein increases the production of alkaline urine, leading to reduced intake of amino acids methionine and stone formation in the kidney patients must avoid increased consumption of foods rich in methionine, such as peanuts, broccoli, mushroom, and cauliflower [2-4]. The restriction of methionine consumption minimizes the risk of cystine crystal formation.

## Prevention of Cystinuriaia

Unfortunately, cystinuria is a genetically inherited complication, which medical practitioners cannot prevent. Clinical facilities or medical practitioners should provide quality health education about cystinuria to promote early diagnosis and treatment. Mainly, medical practitioners should educate community members about cystinuria, its causes, signs and symptoms, and evidence-based pharmacological and non-pharmacological treatment methods. Information about behavioral management will help patients with cystinuria to adhere to health behaviors to avoid adverse signs and symptoms of the complication [2-6]. The medical practitioners should educate community members about the long-term studies of cystinuria patients over the past twenty-one years [2-5]. The education should include information about the importance of early treatment and surgical methods in managing cystinuria [4]. The education will influence patients to seek early treatment and evidence-based care to overcome cystinuria [4].

## Compare and Contrast Themes and Gaps in Literature

The reviewed literature focuses on the pharmacological and non-pharmacological treatment methods for cystinuria. All the selected peer-reviewed selected provide a comprehensive analysis of the pharmacological methods for cystinuria indicate that evidence-based pharmacological methods for cystinuria treatment include urinary alkalization and Cystine-Binding Thiol Drugs (CBTD) like D-penicillamine, tiopronin, captopril, and bucillamine [4]. Examine pharmacological methods for cystinuria treatment consisting of urinary alkalinization and Cystine-Binding Thiol Drugs (CBTD) [3-6]. The medications for cystinuria treatment thoi-based agents and urinary alkalinization. Also, the selected peer-reviewed selected highlights the non-pharmacological methods for cystinuria treatment [1-3]. Dietary modifications and hydration are the main non-pharmacological methods for cystinuria treatment. Additionally, the peer-reviewed articles discuss the effects or benefits of pharmacological and non-pharmacological methods on cystinuria treatment [3-5]. The articles conclude that medicational and non-pharmacological methods treat cystinuria by reducing the formation of new kidney stones in patients [6-7]. On the other hand, the peer-reviewed articles focus on different themes and information about cystinuria [1-4]. The articles by the National Organization for Rare Diseases and the National Kidney Foundation provide comprehensive definitions of cystinuria, signs and symptoms, causes, and treatment and prevention of illness [2]. The articles highlight the evidence-based diagnostics tools for cystinuria, including urinal and imaging tests [1-3]. Discuss only the treatment methods for cystinuria. Also, some peer-reviewed articles detail the side effects of the pharmacological and non-pharmacological treatment methods for cystinuria [5]. Admit the side effects are a high incidence of dose-limiting toxicity and autoimmune disorders [3]. The articles by the National Organization for Rare Diseases and the National Kidney Foundation overlooked the adverse side effects of D-penicillamine. Likewise, provide a detailed discussion of the future concepts in cystinuria treatment [5-6]. The researchers suggest that clinics and medical practitioners should consider new therapies, such as L-cystine dimethyl ester (L-CDME), α-Lipoic acid, and Tolvaptan, in treating and managing cystinuria state that the experiment of Tolvaptan in mice showed that it reduces the concentration of cystine in the urine [3].

## Discussion

An experiment with mice revealed that the α-Lipoic acid therapy increased the solubility of urine cystine, reducing the threat of cystinuria [1-3]. The only researchers that suggested new methods for managing and treating cystinuria. Even though the peer-reviewed articles provide detailed discussions of the pharmacological and non-pharmacological treatment methods for cystinuria, they have failed to provide adequate information on side effects [2-4]. The researchers should offer detailed information on the short and long-term side effects of pharmacological and non-pharmacological treatment methods for cystinuria [2]. The peer-reviewed articles lack accurate dosage of pharmacological methods for managing cystinuria among adults and children suffering from the disease. Also, most of the researchers have not explored the emerging or conventional treatment methods for cystinuria [3-5].

## Questions to further research

- Are L-cystine dimethyl ester (L-CDME), α-Lipoic acid, and Tolvaptan effective approaches for treating and managing cystinuria among adults and children?
- Can medical practitioners incorporate health informatics in managing and treating cystinuria among adults and children?
- Should health facilities and medical practitioners focus on patient and health education to facilitate early diagnosis and treatment of cystinuria among adults and children?

Researchers need to consider the three proposed study questions to facilitate evidence-based cystinuria treatment, access to quality and timely care among adults and children, and reduce medical errors in caring for individuals with cystinuria.

## Conclusion

In conclusion, cystinuria is a rare renal stone disease, which individuals inherit from their family members. The genetic disorder is characterized by gene mutations in SLC3A1 and SLC7A9 and encoding proteins that enhance dibasic amino acid exchange expressed in the proximal tubule of the kidney and the gut. Cystinuria affects approximately one in 7,000 persons in the United States. Individuals with cystinuria experience signs and symptoms, including nausea, vomiting, pain while urinating, blood in the urine, and pain near the abdomen or groin. Untreated cystinuria leads to the blockage of the ureter, urinary tract infections, kidney infections, and bladder or kidney damage. Peer-reviewed articles recommend pharmacological and non-pharmacological treatment methods for cystinuria, including Cystine-Binding Thiol Drugs (CBTD), urinary alkalinization, surgical procedures, dietary modification, and hydration. The evidence-based methods will contribute to early diagnoses and appropriate treatment of cystinuria. Researchers should consider examining the appropriateness of L-cystine dimethyl ester (L-CDME), α-Lipoic acid, and Tolvaptan in treating and managing cystinuria among adults and children.

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