

Effectiveness of Individualized Homoeopathic Medicine in Cases of Urolithiasis: A Prospective Interventional Pre-Post Clinical Trial

Yashasvi Shakdviya^{1,2*}, Mushtaq Ahmed Mhaishale¹, Gaurav Nagar³

¹Parul University Vadodara, Gujarat, India, ²Department of Repertory, University College of Homoeopathy, Dr. S. R. Rajasthan Ayurved University, Jodhpur, India, ³Department of Homeopathic MM, University College of Homoeopathy, Dr. S. R. Rajasthan Ayurved University, Jodhpur, India. *Corresponding Author's Email: yashasvi119@gmail.com

Abstract

Urolithiasis is a result of dehydration, low urine volume or increased excretion of minerals such as calcium, oxalate, etc. It affects approximately 12-15% of the global population, commonly affects third decade of age with predominant male gender incidence. Though considerable advances have happened in the surgical treatment of stone-forming individuals to prevent recurrence, medicinal treatment still requires improvement. This study aimed to assess the role of homoeopathic medicines in management renal colic, dysuria in patients of urolithiasis as well as in reduction of number of stones in urinary tract. In this study male predominance (74.69%) was seen with mean age 37.28 ± 12.525 years. Also, the association of increased body mass index as risk for occurrence of urolithiasis was seen as the 52.04% patients of urolithiasis. In this study frequently indicated medicines were *Lycopodium clavatum*, *Nux vomica*, and *Apis mel*. IHM *Calcarea carb* and *Sarsaparilla* has shown effective results by achieving stone free status. This study concludes that individualized homoeopathic medicines were found effective in significantly reducing renal colic and dysuria and around 50% patients achieved stone free-state during treatment.

Keywords: Clinical trial, Dysuria, Homoeopathic medicine, Renal colic, Urolithiasis.

Introduction

Presence of crystal agglomerates anywhere in the renal system is considered as Urolithiasis or calculi/stone in urinary system (1). According to ICD-11 classification, Urolithiasis is result of dehydration, low urine volume or increased excretion of minerals such as calcium, oxalate, etc. This condition is characterised by the presence of calculi within the urinary system. ICD-11 code GB7Z denotes urolithiasis, unspecified; GB70 & GB71 covers Nephrolithiasis, ureterolithiasis and cystolithiasis (2). Urolithiasis is a common public health issue globally and third most common urological disease that accounts for significant cost, morbidity, and loss of work (3). It affects approximately 12-15% of the global population, with 50% lifetime recurrence risks (4, 5). Many epidemiological studies suggest significant difference in prevalence of urolithiasis as per age, sex, race, diet, geographic, socioeconomic, and climate factors (6). It affects commonly affects third decade of age with predominant male gender incidence (7, 8). Obesity and metabolic diseases

are now considered as risk factors for urolithiasis like calcium oxalate as the dominant component of calculi. In past three decades its prevalence has increased significantly and the recurrence is usually associated with underlying disorder (9, 10). A heterogeneous distribution of renal stones is seen in India as the "stone belt" are Maharashtra (7.6%), Gujarat, Punjab, Haryana, Delhi and Rajasthan whereas southern India has low incidence rate (11). Major shift in lifestyle and dietary habit of high intake of proteins and minerals in the industrialized world increased incidence of urinary stones (12). The crystals are formed due to urinary supersaturation of stone forming salts and low thermodynamic solubility of these salts. The commonest metabolic abnormalities among stone formers is low urine volume (1, 5, 13). Calcium oxalate has been found as the predominant constituent in nephrolithiasis in India (14). Blockage of urine flow causes severe colic and associated with morbidity and renal damage. Current urology practice is targeted

This is an Open Access article distributed under the terms of the Creative Commons Attribution CC BY license (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

(Received 22nd May 2024; Accepted 23rd July 2024; Published 30th July 2024)

primarily for symptomatic management of renal colic, recurrent colic and associated sepsis/ UTI by NSAIDs or IV/ oral ibuprofen or paracetamol and antibiotics combination. Drugs like α -blockers, Ca-channel inhibitors, and phosphodiesterase type 5 inhibitors are used as medical expulsive therapy. Shock wave lithotripsy, minimally invasive percutaneous nephrolithotomy and chemolysis are further treatment as per site, size, type and impact of stone in urinary organs. Though considerable advances have happened in the surgical treatment of stone-forming individuals to prevent recurrence, medicinal treatment still requires improvement (15).

Due to its inexpensive treatment costs and no reported adverse effects, homoeopathy is fast becoming the therapy of choice for the Indian populace. Effective homoeopathic treatment decreases recurrence of stone formation and need for surgical procedures for stone removal (16, 17). Hahnemann's holistic approach states to consider of patient's physical, mental and emotional aspect, causation is taken into consideration for choosing medicine. Many observational and clinical trial studies confirm the effectiveness of homeopathic medicines in urological conditions like urolithiasis (18-24).

Although research and published studies have demonstrated the efficacy of homoeopathic medicines in treating stone cases, no prospective clinical trial with a larger sample size has been carried out at this point to evaluate the role of homoeopathic medicines in managing the symptoms of urolithiasis patients as well as in reducing the size and number of stones in the urinary tract. Thus, for this study, a prospective interventional trial was suggested.

This study was aimed to assess the effectiveness of Individualized Homoeopathic Medicines selected with the help of Synthesis Repertory in cases of urolithiasis by comparing Visual Analogue Scale score for the improvement in symptoms of Renal pain/colic, Dysuria and change in number of stones in urinary tract and achieving stone-free status.

Materials and Methodology

This Prospective interventional study (pre-test & post-test design) was conducted at Dr. MPK Homoeopathic Medical College & Hospital, Jaipur for a period of 18 months out of which cases were registered during first nine months so that minimum nine months follow up can be obtained

from the last case.

Sampling

To calculate the sample size with a prevalence rate of urolithiasis of 15% (25), a confidence level of 95%, and a margin of error of 5%, with considered 10% attrition rate gave the sample size 106. Patients coming to hospital with suggestive signs & symptoms of urolithiasis were screened as per inclusion criteria.

Inclusion Criteria

- Age group: 18-65 years
- Both Sexes
- Patients who gave consent to participate in the study
- Patients diagnosed of Urolithiasis [ICD-11-GB7Z, GB70 & GB71] (2) on the basis of clinical history, examination, X-ray KUB or USG.
- No history of expulsion of calculi after the radiological investigations within one-month period.
- Patients already diagnosed of urolithiasis and taking treatment from other system of medicine but not getting relief and willing to stop previous medicines.

Exclusion Criteria

- Cases with severe hydronephrosis, uremia, recurrent UTI, acute retention of urine for > 24 hours.
- Gross developmental or structural anomaly of kidney.
- Patients who are taking alcohol regularly.
- Pregnant women and Lactating mothers.
- Terminally ill patients.
- Size of calculus more than 15mm were excluded.
- Stag horn calculus was excluded.
- Patients not giving information for the consent to participate in the study.

Dropout Cases

- Consent Withdrawal.
- Poor patient compliance related to habits, diet and medication.
- Medical emergency where patient need surgical intervention or the cases requiring emergency treatment.

Intervention

Single Individualized homoeopathic medicines were selected for each case after proper case taking, analysis of case, evaluation and totality construction followed by Repertorisation with the

help of Synthesis repertory using Radar 10.0 software (26). Each dose consisted of 4 globules (no. 40) medicated with the indicated medicine, advised to be taken orally on a clean tongue with an empty stomach; dosage and repetition depending upon the individual requirement of the cases as per guidelines prescribed by Hahnemann in his 'Organon of medicine' (27). Patients were advised to refrain from handling the globules or from eating, drinking, smoking or brushing their teeth within 30 minutes of taking the globules and were asked to suck the globules, and were asked to suck the globules rather than simply swallowing those. All the medicines and sundry items were procured from a Good Manufacturing Practice (GMP)-certified firm. The selection of potencies was done by strict homoeopathic criteria laid down by different stalwarts. This was done based entirely on the susceptibility of the patient which in turn depends upon nature and duration of illness, severity and peculiarity of the present complaint, intellectual property of the patients, age of the patient and by the degree of the similarity between disease symptoms with that of medicinal symptoms.

Concomitant Care

All the enrolled patients received advice on following general non-medicinal management:

- ◆ Increase water intake.
- ◆ Weight reduction in cases of high BMI/ obesity.
- ◆ Avoiding food articles like nuts and nut products, spinach, wheat bran etc. to reduce oxalate in urine.
- ◆ Reducing Sodium intake.
- ◆ Limiting animal meat intake milk and milk products (28).

Outcome Assessment

- Visual analogue scale score of renal pain/colic and Dysuria: it was measured by asking the patient to circle the number between 0 and 10 measuring the intensity of pain (29).
- Changes in number of stones: Changes were assessed either when patient reported expulsion of stone or at end of three months of follow up by radiological investigation. Subjects who achieved stone free-state were marked.

Selection of Tools

Following provision of patient information sheet in English and Hindi language preliminary screening was performed using inclusion criteria and detailed screening using specified exclusion

criteria then eligible patients were recruited into the trial. Written informed consent was obtained from participants in the study. Case-taking was done in adherence with the standard homoeopathic principles. Eligible patients were properly interrogated, examined and investigated through a standardized case taking proforma. Following analysis and evaluation of symptoms, framing of symptom totality, Repertorisation were done from software-based Synthesis repertory from RADAR software. Repertorial analysis is done with due consultation from Materia Medica. Visual Analogue Score and radiological findings were used for outcome assessment analysis. The Helsinki's declaration on human experimentation was considered during methodology design (30).

Data Collection

The outcomes were assessed at baseline and every month up to 3 months of intervention. Data collected with help of specially designed case taking proforma for primary information of patient, reports of X-ray KUB/USG & urinalysis as per case for confirmation and follow of case for number of stones in urinary tract and VAS score of renal colic & dysuria for outcome assessment of intervention.

Data Analysis and Statistical Techniques

Baseline continuous descriptive data were presented in terms of percentages and mean, standard deviations (SD) etc for sex, BMI status, habit, use of millet and dairy products in diet presented with graphs and tables as appropriate. Continuous data (age, body-mass index) were presented as Mean $\pm$ Standard deviations for age, height, weight, BMI, Daily water intake. The intention to treat (ITT) approach was applied for result analysis. The intra-group changes were presented in terms of descriptive statistics-mean and 95% CI and paired t- Test for VAS score pre-post treatment for renal colic & dysuria and change in number of stones pre-post treatment by using SPSS software (31).

Results

In this study 98 cases (enrolled 106, dropout 08) were considered for data analysis for outcome measures as they maintained follow ups. Mean age recorded was 37.28 ± 12.525 years (Table 1). The mean height and weight of the study participant was 170.73 ± 8.835 cms. and 76.23 ± 11.152 kgs.

The mean BMI was 26.147 with SD 3.387 as shown in Table 1. The daily water intake of maximum participants was moderately adequate i.e. mean intake was 3.306 lts. /day with SD of 0.836.

In this study, it was found that 52.04% were overweight and 14.29% were obese as per their BMI status whereas 32.65% had normal body weight (Figure 1).

Table 1: Demographical details of the study participant at Baseline

	N	Minimum	Maximum	Mean	Std. Deviation
Age	98	18	64	37.28	12.525
Height	98	153	188	170.73	8.835
Weight	98	45	93	76.23	11.152
BMI	98	17.57813	32.21176	26.1476575	3.38777925
Daily water intake in liters	98	2.00	5.00	3.3061	0.83614
Valid N (listwise)	98				

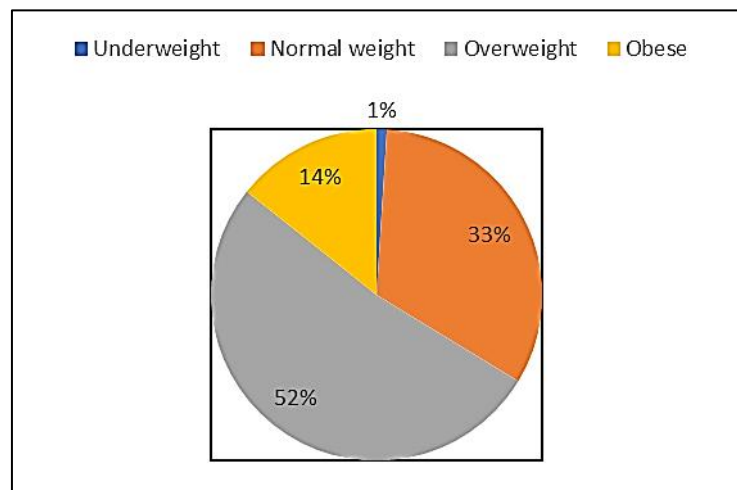


Figure 1: Pie Chart Showing Incidence as per BMI Status of Study Participants

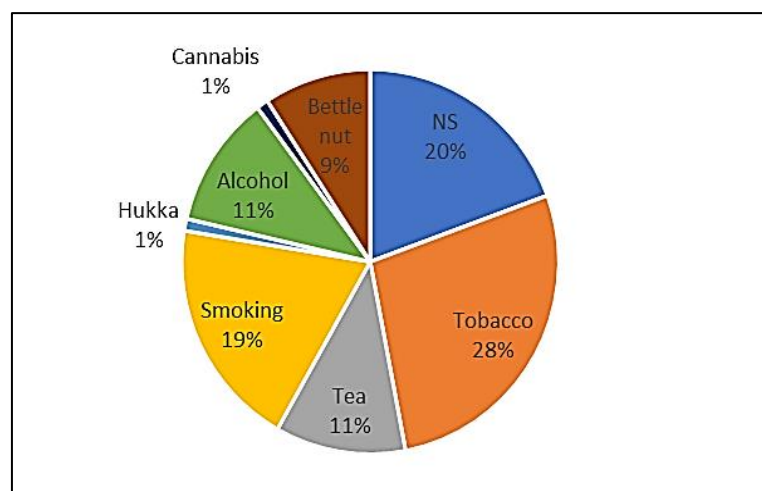


Figure 2: Pie Chart Showing Habits of Study Participants

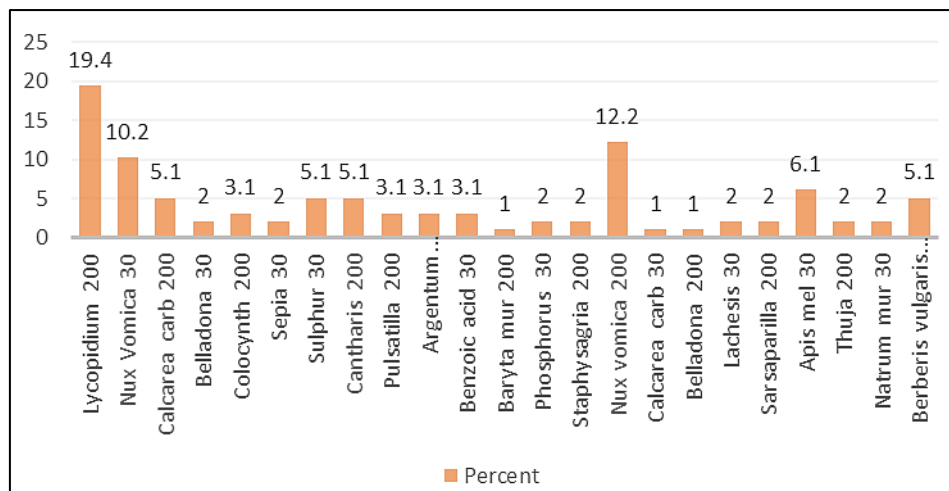


Figure 3: Bar Graph Showing IHM Prescribed for Study Participants

In this study, maximum participants i.e. 27.55% had tobacco chewing habit, 19.39% smoking habit, tea & alcohol in 11.22%, 9.16% beetle nut use, 1.02% cannabis and hukka habit while rest 19.39% reported no habits/ addictions as shown in (Figure 2).

In this study individualized homoeopathic medicine *Lycopodium clavatum* was prescribed to

19.39% cases followed by *Nux vomica* in 10.20%, *Apis mellifica* in 06.12%. Other IHM found useful were *Benzoic acid*, *Argentum nitricum*, *Pulsatilla nigrican*, *Colocynthis*, *Natrum mur*, *Thuja*, *Sarsaparilla*, *Lachesis*, *Staphysagria*, *Phosphorus*, *Sepia* and *Belladonna*, *Calcarea carb*, and *Baryta mur* (Figure 3).

Table 2: Paired t-Test Statistics, Paired Samples Statistics

Group			Mean	N	Std. Deviation	Std. Error Mean
IHM	Pair 1	Renal colic VAS scale pre-treatment	6.95	98	2.459	0.248
		Renal colic VAS scale post- treatment	0.95	98	1.029	0.104
	Pair 2	Dysuria VAS scale pre-treatment	6.64	98	2.290	0.231
		Dysuria VAS scale post-treatment	1.41	98	1.147	0.116
	Pair 3	Change in number of stone pre-treatment	2.59	98	1.572	0.159
		Change in number of stone post-treatment	0.76	98	0.886	0.089

Table 3: Paired t-Test Statistics, Paired Samples Test

Group			Paired Differences						Sig. (2-tailed)		
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t			df
						Lower	Upper				
IHM	Pair 1	Renal colic VAS scale pre- treatment - Renal colic VAS scale post- treatment	6.000	2.306	0.233	5.538	6.462	25.753	97	0.000	
	Pair 2	Dysuria VAS scale pre- treatment - Dvsuria VAS scale	5.235	1.904	0.192	4.853	5.616	27.219	97	0.000	

	post- treatment								
Pair 3	Change in number of stone pre- treatment - Change in number of stone post- treatment	1.837	1.412	0.143	1.554	2.120	12.877	97	0.000

As shown in Table 2 and 3, a paired t-test was conducted on the renal colic VAS scale before and after treatment. The calculated mean for the pre-treatment scale was 6.95 [SD $\pm$ 2.459] and for the post-treatment scale, the mean was 0.95 [SD $\pm$ 1.029]. The paired difference t statistic is 25.753, with an asymptotic significant value of 0.000 (p-value < 0.001). This means a significant statistical difference between the renal colic VAS scale pre-treatment and post-treatment.

For Dysuria VAS scale before and after treatment, the calculated mean for the pre-treatment scale was 6.64 [SD $\pm$ 2.290] and for the post-treatment scale, the mean was 1.41 [SD $\pm$ 1.147]. The paired difference t statistic is 27.219, with an asymptotic significant value of 0.000 (p-value < 0.001). Hence, Dysuria VAS scale pre-treatment and post-treatment have significant differences.

For Change in number of stones before and after treatment, the calculated mean for the pre-treatment scale was 2.59 [SD $\pm$ 1.572] and for the post- treatment scale, the mean was 0.76 [SD $\pm$ 0.886]. The paired difference t statistic is 12.877, with an asymptotic significant value of 0.000 (p-value < 0.001). Thus, the change in number of stone pre- treatment and post-treatment was statistically significant. Whereas in total 49 patients i.e. 50% of patients achieved stone free-state.

Discussions

Similar to epidemiological studies, in this study male predominance (74.69%) was seen with mean age 37.28 $\pm$ 12.525 years.^{1,2,3,8} In this study the association of increased body mass index as risk for occurrence of urolithiasis was seen as the 52.04% patients of urolithiasis were overweight with high BMI (M =26.1476575; SD $\pm$ 3.387, 5, 6, 10, 13).

Geographical condition and climate of site of study (Jaipur, Rajasthan) favors fluid loss due to dry hot climate as well as dietary habits of millet and dairy product use i.e. 47.96% were regular users were strong factors associated with the higher incidence in this study (7, 9-12).

Individualized homoeopathic medicines were selected in the study after detailed case taking and case processing as per homoeopathic principles with help of Synthesis repertory. Each patient received IHM with auxiliary management instructions. Out of 98 cases, 50% (n=49) patients achieved Stone free status during treatment. Out of these 49 stone free patients, 16 received IHM *Lycopodium clavatum* also this was most frequently indicated curative medicine in the study i.e. 19.39% patients received this medicine. Homoeopathic clinical trials and case reports also suggest *Lycopodium clavatum* as most indicated homoeopathic medicine for urolithiasis (20, 23). Other than this *Nux vomica* was second most frequently prescribed medicine with 3 cases of stone free status but all 6 cases who received *Apis mel* reported expulsion of stones. *Calcarea carb* and *Sarsaparilla* has shown effective results by achieving stone free status. In the study IHM were effective in reducing VAS score of renal colic and dysuria showing symptomatic relief in patients as well as in expulsion and reducing number of stones on patients (18-24). Our findings also corroborate with other such studies. If the study had been conducted over a longer period of time with a bigger sample size, more significant findings would have been obtained. This study does not have the capacity to report on the homoeopathic literature's suggestion that homoeopathic medicines also reduce the recurrence rate of stone formation time. Integrated informed decision to patient of urolithiasis could be a better approach where a fresh case can start with homoeopathic treatment and to delay or devoid surgery as far as possible. Such practice will not only provide a better and safe informed clinical option to patient but overall reduces cost and treatment time in patient population of developing country like India.

Conclusion

In general practice of homoeopathy, urolithiasis is one of the most common referred condition. Recently published researches also support an effective role of IHM in urological disorders especially urolithiasis. In this study individualized

homoeopathic medicines were found effective in significantly reducing renal colic as well as calculi related dysuria. Almost 50% patients achieved stone free-state during treatment which establishes role of IHM in expulsion of stones in patients of urolithiasis. Thus, it may be concluded that homoeopathic treatment is effective treatment modality for urolithiasis and future studies of longer duration with robust methodology like randomized controlled trials and STONE score which assess metabolic factors also, may further establishing substantiate role of homoeopathic medicine in urolithiasis cases.

This study reveals that homoeopathic drugs can help urolithiasis patients become stone-free and offer an alternative to invasive treatment options. Thus, early detection and homoeopathic intervention not only decreases patient care costs by avoiding surgical treatment wherever possible, but it can also be relied on as the first line of treatment in cases of urolithiasis. This study also shown the usefulness of homoeopathic drugs such as *Sarsaparilla*, *Apis mel*, and *Calecarea carb* in aiding stone passage, which had not previously been described in materia medica literature.

Abbreviations

ICD-11: International Classification of Diseases

GB: ICD code for urolithiasis

UTI: Urinary Tract Infection

NSAID: Non-steroidal anti-inflammatory drugs

IV: IntraVenous

KUB: Kidney, Ureter & Bladder

USG: Ultra-SonoGraphy

GMP: Good Manufacturing Practice

BMI: Basal metabolic rate

SD: Standard Deviations

ITT: Intention To Treat

VAS: Visual Analogue Scale

CI: Confidence Interval

IHM: Individualized Homoeopathic Medicine

STONE score: Size, Topography (location of stone), Obstruction, Number of stones present, and Evaluation of Hounsfield Units.

Acknowledgement

The authors sincerely acknowledge Parul University, Vadodara for approval of this study and Homoeopathy University Jaipur for ethical approval of the study and data collection. We are thankful to all PhD cell and DRC members of both institute for improving the methodology by their

valuable inputs and administrative support. We are thankful to Mr. R.K. Kherra, Statistical Assistant, Simbi labs for statistical assistance. We acknowledge contribution of all the participants of the study.

Author Contributions

Yashasvi Shakdvipiya: Concept, design, data collection, analysis and manuscript writing; Mushtaq Ahmed Mhaishale: Concept, design, and manuscript writing; Gaurav Nagar: Data analysis and manuscript writing.

Conflicts of Interest

None declared.

Ethics Approval

Ethical clearance was obtained from Institutional Ethical Committee of University Ref no. HU/2020/2356/F dated 25/01/2020 for methodology of the study.

Funding

Nil.

References

1. Stamatelou K, Goldfarb DS. Epidemiology of Kidney Stones. *Healthcare*. 2023 Jan 1;11(3):424.
2. World Health Organisation. ICD-11. International Classification of Diseases 11th Revision. 2022. Available from: <https://icd.who.int/en>.
3. Romero V, Akpınar H, Assimos, DG. Kidney stones: A global picture of prevalence, incidence and associated risk factors. *Rev Urol*. 2010 Spring; 12(4):e86-96.
4. Chauhan CK., Joshi MJ. Growth inhibition of Struvite crystals in the presence of juice of Citrus medica Linn. *Urological research*. 2008 Sep 16;36:265-273. DOI: <https://doi.org/10.1007/s00240-008-0154-4>
5. Semins MJ, Matlaga BR. Medical evaluation and management of urolithiasis. *Therapeutic Advances in Urology*. 2010 Feb;2(1):3-9.
6. Chewcharat A, Curhan G. Trends in the prevalence of kidney stones in the United States from 2007 to 2016. *urolithiasis*. 2021 Feb;49(1):27-39. Available from: <https://doi.org/10.1007/s00240-020-01210-w>
7. Edvardsson VO, Indridason OS, Haraldsson G, Kjartansson O, Pálsson R. Temporal trends in the incidence of kidney stone disease. *Kidney International*. 2013 Jan;83(1):146-52.
8. Gilliams K, Juliebo-Jones P, Juliebo S, et al. Gender differences in kidney stone disease (KSD): findings from a systematic review. *Curr Urol Rep*. 2021;22(10):50.
9. Liu Y, Chen Y, Liao B, Luo D, Wang K, Li H, et al. Epidemiology of urolithiasis in Asia. *Asian Journal of Urology*. 2018 Oct;5(4):205-14.

10. Moe OW. Kidney stones: pathophysiology and medical management. *The Lancet*. 2006 Jan;367(9507):333-44.
11. Mikawlawng K, Kumar S. Current scenario of urolithiasis and the use of medicinal plants as antiurolithiatic agents in Manipur (North East India): A Review. *International Journal of Herbal Medicine*. 2014;2(1):1-12.
12. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. See Editorial by Goldfarb, p. 1951. *Kidney International*. 2003 May 1;63(5):1817-23.
13. Khan SR, Canales BK. Genetic basis of renal cellular dysfunction and the formation of kidney stones. *Urological Research*. 2009 Aug 1;37(4):169-80.
14. Kumar A. An increase incidence in uric acid nephrolithiasis: changing patterns. *Journal of Clinical and Diagnostic Research*. 2016;10(7):BC01-BC03.
15. EAU Guidelines. Edn. presented at the EAU Annual Congress Paris 2024. ISBN 978-94-92671-23-3.
16. Prasad R. Homoeopathy booming in India. *The Lancet*. 2007 Nov;370(9600):1679-80.
17. Singh P, Yadav RJ, Pandey A. Utilization of indigenous systems of medicine & homoeopathy in India. *The Indian Journal of Medical Research [Internet]*. 2005 Aug 1;122(2):137-42.
18. Gupta G, Nayak C, Sexena R, Kumar A. Role of homoeopathic prescribing methodology in the treatment of urolithiasis: a case report. *Indo American Journal of Pharmaceutical Research*. 2018;8(07): 1473-1279.
19. Sharma S, Wadhvani GG. Experience with homoeopathy in a case of large urethral calculus. *Indian Journal of Research in Homoeopathy*. 2013; 7(4): 176-80.
20. Siddiqui VA, Singh H, Gupta J, Nayak C, Singh V, Dixit R, et al. A multicenter observational study to ascertain the role of homoeopathic therapy in Urolithiasis. *Indian Journal of Research in Homoeopathy*. 2011; 5(2): 30-39.
21. Gupta AK, Gupta J, Siddiqui VA, Mishra A. A Case Record: A big urinary calculus expelled with homoeopathic medicine. *Indian Journal of Research in Homoeopathy*. 2008; 5(2): 50-55.
22. Sumithran PP. Case of multiple urinary Calculi. *Indian Journal of Research in Homoeopathy*. 2016; 2(10): 99.
23. Chakma A. Renal Calculi: An Evidence Based Case Study. *Journal of Applied Research*. 2015; 7(1): 227- 234.
24. Ganesan T, Ravi DB, Vasavan J, Khurana A, Nayak D, Periandavan K. Homoeopathic preparation of *Berberis vulgaris* as an inhibitor of Calcium oxalate crystallization: An in vitro evidence. *Indian Journal of Research in Homoeopathy*. 2015; 15(9): 2-17.
25. Guha M, Banerjee H, Mitra P, Das M. The Demographic Diversity of Food Intake and Prevalence of Kidney Stone Diseases in the Indian Continent. *Foods*. 2019 Jan 21; 8(1):37. DOI: 10.3390/foods8010037.
26. Schroyens F. RADAR software. Synthesis Repertory. Version 10.0. Zeus soft: Namur, Belgium. <https://www.radaropus.com/support/download>
27. Hahnemann S. *Organon of Medicine*, 6th ed. New Delhi: B. Jain Publishers (P) Ltd.; 2019.
28. Taylor EN, Fung TT, Curhan GC. DASH-Style Diet Associates with Reduced Risk for Kidney Stones. *Journal of the American Society of Nephrology*. 2009 Aug 13;20(10):2253-9.
29. Hayward M. Pain: clinical manual for nursing practice. *Nursing Standard*. 1994 Dec 7;9(11):55-5.
30. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bulletin of the World Health Organization*. 2001;79(4):373-4.
31. Statistical package for social sciences. Version 20.0. IBM SPSS statistics for Windows, Armonk, New York, United States. <https://www.ibm.com/spss>