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**Short Communication**

# Calcium carbonate urolithiasis in a diabetic pet rabbit fed with high dietary calcium- Causal effect study and its surgical management

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## Abstract

**A nine years old New Zealand White female diabetic rabbit (blood glucose level~300 mg/dL) was presented to the Out Patient Department (OPD) of Veterinary Clinical Complex, Kolkata, India with a history of chronic weight loss along with inappetence, polyuria, haematuria from last 10 days. Feeding history revealed that the animal was maintained with a mixed diet that is rich in calcium (Ca). Manual examination revealed moderate pain near the caudal abdominal region, and a hard mass was palpated at the level of the urinary bladder. Straight lateral radiograph of the abdomen showed the presence of radiodense cystolith. Hence, cystotomy was done, and the rabbit recovered uneventfully. The analysis of the stone revealed calcium carbonate as a major content. The present article describes successful surgical management of urolith in a rabbit and confers ample evidence that high calcium diet, peculiar Ca metabolism along with higher intake of carbohydrates that increase the risk of diabetes, may setup urolithiasis. The present study also emphasises the fact that diminished Na+-K+-ATPase activity in diabetes can play a pivotal role in the pathogenesis of peripheral vascular and neural complications leading to the development of bladder dysfunction, diminished urine flow in diabetic rabbits resulting in nidus formation and thereby further accumulation of calcium salts in and around nidus leads to the formation of urolithiasis.**

**Keywords:** Calcium carbonate, Cystolith, Diabetes, Rabbit, Surgery

## Highlights

- Cystotomy
- Calcium carbonate stone
- Diabetes mellitus
- Gradual dietary modifications
- Uneventful recovery

Study on urolithiasis in rabbits has been gaining an increased interest by veterinarians (Kucera *et al.*, 2017). In many households, rabbits are treated as per their canine and feline pets in terms of attention and love. Hence, demand for better and expertise veterinary services for these pet rabbits is the need of the hour by these owners (Linton, 2023). Therefore, together this increasing popularity along with suboptimal husbandry conditions for several of them (Rooney *et al*., 2014), veterinarians have to face more and more number of urolithiasis cases in future (Mota-Rojas *et al*., 2023). Several case reports on urolithiasis of rabbits have been reviewed (Reavill and Lennox, 2020; Smith, 2021). Most of the literatures as published found that calcium is the predominant stone in rabbit uroliths; hence, calcium metabolism and association between serum calcium and dietary provision must be looked into for analysis of development of such liths (Sorensen, 2014). In rabbits, uroliths and nephroliths develop because of their peculiar calcium (Ca) metabolism, characterised by high gut absorption of Ca and high blood levels with increased excretion of surplus Ca in urine predisposing for the development of calcium-containing stones (Pak, 2012; Varga, 2014).

Diabetes mellitus causes malfunction of the Urinary bladder in nearly 50% of the patients (Liu and Daneshgari, 2014; Erdogan *et al*., 2022) due to primarily of afferent neuropathy and secondarily to efferent neuropathy. These pathological condition leads to development of atony of urinary bladder and urine retention (Wang *et al*., 2020). Precipitation of excess calcium sludge in urine together with diminished urine flow in diabetic rabbits results in the development of nidus and thereby further accumulation of calcium salts in and around the nidus, leading to the formation of urolithiasis.

A New Zealand White female rabbit was presented to the OPD of Veterinary Clinical Complex, Kolkata, India with a history of chronic weight loss and diabetes mellitus (blood glucose level~300 mg/dL) along with inappetence, polyuria, haematuria from last 10 days. The history of feeding habit was enquired and found that the animal had a habit of taking lettuce (19 gms Ca/50 gms), lentils (40 mg Ca/80 gm raw), beans (50 mg Ca/90 gm),

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potatoes (20 gm Ca/250 gms boiled), apple (6 gm Ca/120 gms), banana (12 gms/150 gms), broccoli (100 gms Ca/ 120 gms), carrots (40 gm Ca/120 gms) and tomatoes (15 gms Ca/120 gms) on an average as mixed diet.

All the physiological parameters like temperature, pulse, respiration, and $O_2$ saturation were within the normal range. Physical examination revealed moderate pain in the lower abdomen. A hard mass was palpated at the bladder region. To differentiate between atonic bladder with cystitis and urolithiasis, a straight lateral radiograph of the lower abdomen was taken. X-ray shows a radio-dense structure with serrated margin at the upper outer border of urinary bladder (Fig. 1). The case was diagnosed as cystolith. A routine urine culture was done and found negative for any microbial growth. Routine blood parameters were done and planned for cystotomy.

Body weight of the rabbit was 2.2 kg. The animal was anaesthetized with the combination of xylazine HCl @ 5 mg/kg body weight and ketamine HCl @ 30 mg/kg body weight through deep intramuscular route. The animal was placed in dorsal recumbency, and an intravenous 26 gauge butterfly needle was placed to provide fluids. Routine aseptic preparation of the surgical site was done. A caudal mid ventral incision was made, and the bladder was exteriorized. A stab incision was made, and suction was inserted into the bladder to remove all the urine. The incision was extended further, and the stone was removed (Fig. 2) by using a gall spoon. The bladder-urethral junction was occluded, and sterile saline was flushed several times through a 6FG infant feeding tube (Fig. 3). The bladder was then copiously lavaged with lukewarm sterile saline and sutured by lembert technique using absorbable Trugut® Chromic Catgut (USP 3-0) as suture material. The abdominal cavity was lavaged with lukewarm sterile saline and sutured by simple interrupted pattern using absorbable VICRYL® 3-0 (Braided Coated Polyglactin 910) as suture material. Cutaneous wound was closed using Linex® 2-0 (Monofilament Polyamide Nylon) by simple interrupted suture pattern (Fig. 4). Removed stone was submitted for chemical analysis. Mupirocin ointment was applied locally, and a protective bandaging was done. Systemic antibiotic (enrofloxacin @ 5 mg/kg body weight) was given once daily intramuscularly for 5 days, and non-steroidal anti-inflammatory drug (meloxicam @ 0.3 mg/kg body weight) once daily subcutaneously for 3 days was given.

The rabbit was recovered uneventfully, and cutaneous stitches were removed after 10 days. The basic diet for a mature, non-pregnant, non-lactating pet rabbit should be a balanced ration containing high fibre (~18%) including pelleted feed, grass hay, leafy green vegetables, and a limited amount of treat foods such as oats, bread and fruits (Hillyer, 1994).

The role of diet in the incidence of urolithiasis is not clear; however, it is postulated that there is a positive correlation between occurrence of urolithiasis and high calcium diet. The normal recommended allowance of calcium for rabbit is ~5 g/kg as maintenance and ~8 g/kg for growth and lactation (Kamphues, 1985). There is a peculiarity in calcium metabolism in rabbit that the excess dietary calcium is absorbed from the intestine and that excess amount is being excreted through urine, hence the amount of sludge is excessive in rabbits fed on high-calcium diet (Kamphues *et al*., 1986; Katona *et al*., 2004; Clauss and Hummel, 2008). From the diet history of the rabbit, it is clear that the animal was on hypercalcemic diet and hence, may be predisposed to the development of urolithiasis. However, it has also been documented by Prebble (2014) and Smith (2013) that wild rabbits are adapted to high calcium load in their diet even after consuming high proportion of legumes in their diet as natural forage. Hence, only high calcium diet may not be the only factor for the development of urolithiasis, rather other factors altogether contribute to the same.

The analysis of the stone revealed calcium carbonate as content. It was pertinent that there was high urine calcium sludge over a long period of time, but along with that, the overflow incontinence and delayed evacuation must had been a contributory factor. The rabbit was diabetic and therefore may develop atony of the bladder. Diminished Na+-K+-ATPase activity in diabetes has been proposed to play a role in the pathogenesis of peripheral vascular and neural complications leading to the development of bladder dysfunction (Greene *et al*., 1987; Winegrad, 1987). Hence, it may be derived that these two factors' interplay precipitated the present surgical condition. The rabbit was not treated with any anti-diabetic drugs (Roth *et al*., 1980; Conaway *et al.*, 1981; Roman-Ramos *et al*., 1995; Catala *et al*., 2001) and was recovered uneventfully without any complications for six follow-up months. Some diet modifications were advocated as more vegetables which are low in calcium, such as carrots, lettuce, cucumber, apple and fresh grass. Dietary changes were introduced gradually over a number of days to minimize the potential for the development of diarrhoea. The owner was instructed to give their pet rabbit plenty of fresh water and green leafy vegetables in order to keep the urine diluted. The owner was also recommended to offer hay constituting 80–90% of daily nutritional intake in order to increase water consumption. It was also advised to allow plenty of time outside the cage for exercise in order to promote regular urine and prevent weight gain.

**Calcium carbonate urolith in diabetic rabbit**

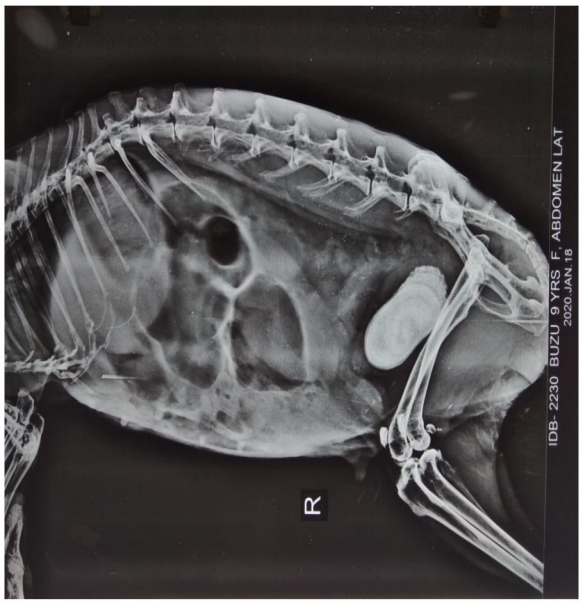


**Fig. 1. Diagnosis of cystolith through X-ray**

**Fig. 2. Incision over bladder to remove the urolith**

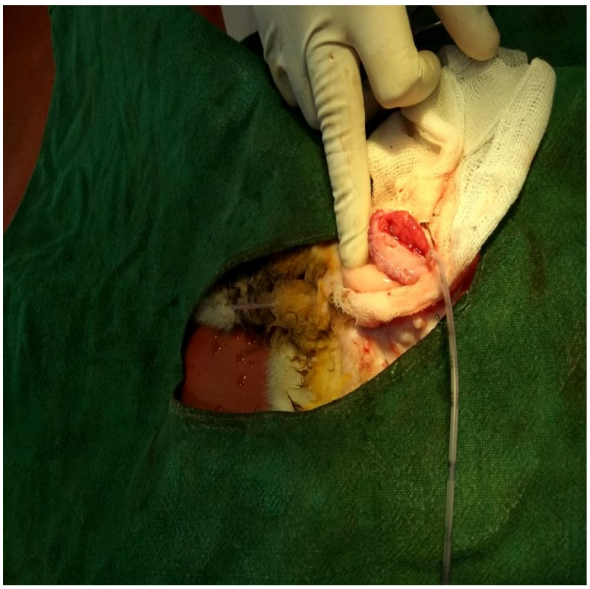

**Fig. 3. Passing of urinary catheter**

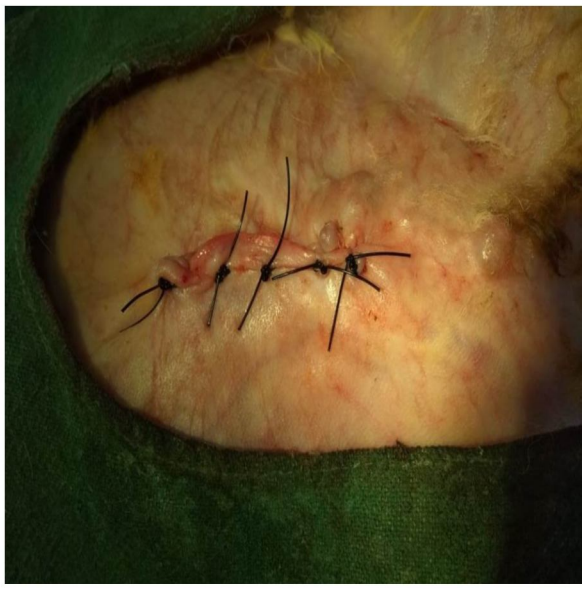

**Fig. 4. Closure of skin wound**

A high calcium diet along with more carbohydrate predisposing to diabetes may set up urolithiasis in rabbits. Early diagnosis of the disease and proper decisions in achieving the goal is the key to success on which the treatment and outcome of the patient depends.

**Conflict of interest:** The authors declare that there is no conflict of interest in this manuscript.

**Author's contribution:** CMT, PM: Data collection, surgical operation, manuscript preparation; SR: Manuscript preparation and scientific inputs; SSK: Diagnostic backup and manuscript preparation.

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**REFERENCE**

Catala J, Daumas M, Chanh AP, Lasserre B and Hollande E, 2001. Insulin and glucagon impairments in relation with islet cells morphological modifications following long term pancreatic duct ligation in the rabbit- A model of non-insulin-dependent diabetes. Int J Exp Diabetes Res, 2(2): 101-112, doi: 10.1155/edr.2001.101

Clauss M and Hummel J, 2008. Getting it out of the (digestive) system: hindgut fermenters and calcium. In: 7th Biennial Symposium of the Comparative Nutrition Society, Liscomb Mills, Nova Scotia, 8 August 2008 - 13 August 2008. Comparative Nutrition Society, pp 30-36, doi: 10.5167/uzh-3539

Conaway HH, Faas FH, Smith SD and Sanders LL, 1981. Spontaneous diabetes mellitus in the New Zealand White rabbit: physiologic characteristics. Metabolism, 30(1): 50-56, doi: 10.1016/0026-0495(81)90218-3

Erdogan BR, Liu G, Arioglu-Inan E and Michel MC, 2022. Established and emerging treatments for diabetes-associated lower urinary tract dysfunction. Naunyn-Schmiedeberg's Arch Pharmacol, 395(8): 887-906, doi: 10.1007/s00210-022-02249-9

Greene DA, Lattimer SA and Sima AAF, 1987. Sorbitol, phosphoinositides and sodium-potassium- ATPase in the pathogenesis of diabetic complications. N Eng J Med, 316(10): 599-606, doi: 10.1056/NEJM198703053161007

Hillyer EV, 1994. Pet rabbits. Vet Clin North Am Small Anim Prac, 24(1): 25-65, doi: 10.1016/S0195-5616(94)50002-0

Kamphues J, 1985. Energy and nutrients requirements of pregnant rabbits. Zuchtungskunde, 56: 207-222

Kamphues J, Carstensen P, Schroeder D, Meyer H and Schoon HA, 1986. Effects of increasing calcium and vitamin D supply on calcium metabolism of rabbits. J Anim Physiol Anim Nutr, 56: 191-208

Katona K, Biro Z, Hahn I, Kertesz M and Altbacker V, 2004. Competition between European hare and European rabbit in a lowland area, Hungary: A long-term ecological study in the period of rabbit extinction. Folia Zoologica, 53(3): 255-268

Kucera J, Koristkova T, Gottwaldova B and Jekl V, 2017. Calcium sulfate dihydrate urolithiasis in a pet rabbit. J Am Vet Med Association, 250(5): 534-537, doi: 10.2460/javma.250.5.534

Linton C, 2023. Barriers between Client Education/Communication and Exotic Animal Husbandry. Honors College Theses, Murray State University

Liu G and Daneshgari F, 2014. Diabetic bladder dysfunction. Chin Med J (Engl), 127(7): 1357-1364

Mota-Rojas D, Whittaker AL, de la Vega LT, Ghezzi M and Lezama-García K, 2023. Veganism and animal welfare, scientific, ethical, and philosophical arguments. J Anim Behav Biometeorol, 11: e2023015, doi: 10.31893/jabb.23015

Pak C, 2012. Calcium Urolithiasis: Pathogenesis, Diagnosis, and Management. Springer Science and Business Media

Prebble J, 2014. Nutrition and feeding. In: BSAVA Manual of Rabbit Medicine. BSAVA Library, pp 27-35, doi: 10.22233/9781910443217.3

Reavill DR and Lennox AM, 2020. Disease overview of the urinary tract in exotic companion mammals and tips on clinical management. Vet Clin North Am Exot Anim Prac, 23: 169-193, doi: 10.1016/j.cvex.2019.09.003

Roman-Ramos R, Flores-Saenz JL and Alarcon-Aguilar FJ, 1995. Anti-hyperglycemic effect of some edible plants. J Ethnopharmacol, 48(1): 25-32, doi: 10.1016/0378-8741(95)01279-m

Rooney NJ, Blackwell EJ, Mullan SM, Saunders R and Baker PE *et al*., 2014. The current state of welfare, housing and husbandry of the English pet rabbit population. BMC Res Notes, 7: 942, doi: 10.1186/1756-0500-7-942

Roth SI, Conaway HH, Sanders LL, Casali RE and Boyd AE, 1980. Spontaneous diabetes mellitus in the New Zealand White rabbit: preliminary morphologic characterization. Lab Invest, 42(5): 571-579

Smith MV, 2013. Textbook of rabbit medicine. Elsevier Health Sciences

Smith MV, 2021. Diagnosing and treating urinary tract disease in rabbits. In Pract, 43(3): 143-151, doi: 10.1002/inpr.28

Sorensen MD, 2014. Calcium intake and urinary stone disease. Transl Androl Urol, 3(3): 235-240, doi: 10.3978/j.issn.2223-4683.2014.06.05

Varga M, 2014. Chapter 1 - Rabbit Basic Science, In: Varga, M. (Ed.), Textbook of Rabbit Medicine (Second edn.). Butterworth-Heinemann, pp 3-108, doi: 10.1016/B978-0-7020-4979-8.00001-7

Wang CC, Jiang YH and Kuo HC, 2020. The pharmacological mechanism of diabetes mellitus-associated overactive bladder and its treatment with botulinum toxin A. Toxins, 12(3): 186, doi: 10.3390/toxins12030186

Winegrad AI, 1987: Does a common mechanism induce the diverse complications of diabetes? Diabetes, 36(3): 396-406, doi: 10.2337/diab.36.3.396

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