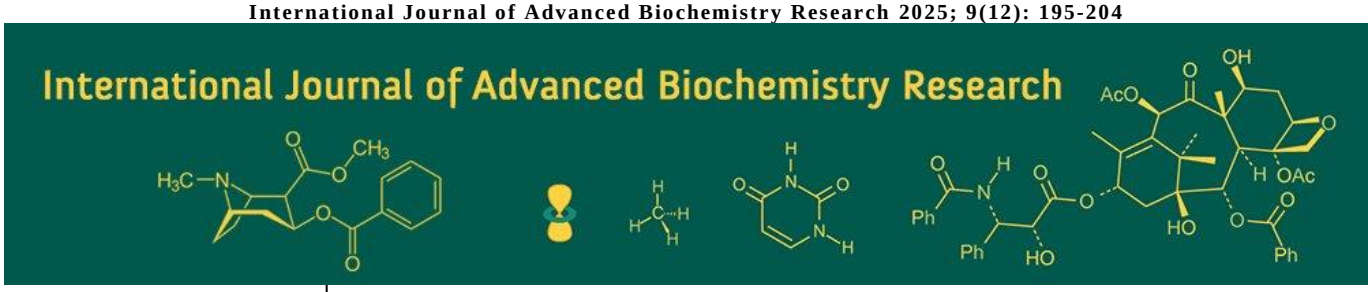

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Prevalence and therapeutic evaluation of using *Serum anguillae* and *Urea pura* in management of chronic kidney disease in dog

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Abstract
The present study was conducted to assess the prevalence, haemato-biochemical and nephrosonographic alterations, and to compare the therapeutic efficacy of homeopathic and conventional medicines in dogs suffering from chronic kidney disease (CKD). Forty CKD-affected dogs, irrespective of age, breed or sex, presented at the Veterinary Clinical Complex, College of Veterinary Science, Khanapara, were randomly allocated into two groups (n=20 each). Group A received homeopathic formulations *Serum anguillae* 6X and *Urea pura* 30CH while Group B was administered conventional drugs (Rkleen and Renodyl). The overall prevalence of CKD was found to be 1.25%, with the highest incidence observed in Labrador Retrievers (0.64%) and dogs aged above 6 to 10 years (0.72%). Common clinical manifestations included inappetence, vomiting, polyuria, polydipsia, diarrhoea, pale mucous membranes, dehydration, lethargy, weight loss and haematuria. Haemato-biochemical evaluations revealed leukocytosis, elevated serum creatinine, BUN, phosphorus and potassium, along with decreased albumin and chloride levels. Urinalysis indicated proteinuria and increased urine protein-to-creatinine ratio. Nephrosonographic changes comprised increased cortical echogenicity, thickened renal cortices, loss of corticomedullary differentiation and wavy renal capsule. Both homeopathic and conventional therapies were found to be equally effective in managing CKD stages II and III, with homeopathy offering added economic advantage and no observed adverse effects. However, cases of stage IV CKD showed poor response to either therapeutic modality.

Keywords: Chronic kidney disease, dog, homeopathy, *Serum anguillae*, *Urea pura*, conventional treatment

Introduction
To understand abnormalities in homeostasis, it is essential to first consider normal kidney function and how it is affected by renal disease. The kidneys are specialized organs that perform a variety of vital functions. Their primary role is filtration retaining essential substances while excreting toxic and unnecessary metabolic waste products into the urine. These functions become impaired in kidney diseases. Chronic kidney disease (CKD) is a progressive and long-standing pathological condition, defined by the presence of structural and/or functional abnormalities in one or both kidneys, persisting for a duration of at least three months (Polzin, 2011) [32]. The development of this progressive disease increases with age (Perez *et al*., 2018) [31] and is characterized by different stages of architectural abnormality of the renal parenchyma, with or without clinically evident functional impairment (Constantinescu *et al*., 2015) [8]. CKD is considered the most common form of kidney disease in dogs. Early detection of the disease is of utmost importance. The most notable uraemic signs include gastrointestinal symptoms such as inappetence, vomiting, halitosis, ulcerations on the oral mucosa, uraemic stomatitis, tongue tip necrosis, and melena or haematochezia (Kumar *et al*., 2020; Nakang, 2017; Tufani *et al*., 2017) [22, 28, 42]. Other common clinical signs include dullness, lethargy, weight loss, cachexia, hypertension, and anaemia. Cardiovascular disease and renal osteodystrophy may also develop as complications. Urine production may vary depending on the etiology and stage of the disease (Foster, 2013; Sheeran, 2021; Mishra, 2019; Chew *et al*., 2011) [13, 37, 27, 6]. Conventional therapy for CKD that lessens morbidity and increases survival in affected pets includes the restoration of hydration status and electrolyte balance, correction of anaemia,

management of proteinuria and systemic hypertension, as well as supportive treatment for associated clinical symptoms. However, the medical management of renal failure is often a long and complicated process, with its success largely depending on the cost of treatment, available resources, and the owner's commitment. Research suggests that pets with CKD can achieve a reasonable life expectancy if the condition is detected early and appropriately managed. Complementary and alternative therapies are increasingly being explored in veterinary practice, either in combination with conventional therapy or as stand-alone treatment strategies. A survey conducted by the American Animal Hospital Association reported that 21% of pet owners sought alternative medicine as a treatment option for their pets (Vockeroth, 1999) [44]. One such alternative approach is homeopathy, which follows the "law of similars," stating that substances capable of producing specific symptoms in healthy individuals can be used to treat similar symptoms in sick individuals (Boericke, 2008) [3]. Homeopathy's gentle and safe approach aligns with a fundamental principle of medical intervention that it should not cause harm (Chavelikar *et al*., 2016) [5]. By integrating homeopathy with conventional medicine, there is potential for enhanced therapeutic outcomes. However, there is limited literature available on the treatment of CKD with homeopathic medicines, particularly in the northeastern region. Hence, considering the above, this systematic study was undertaken to evaluate the comparative efficacy of homeopathic and conventional medicines in the management of chronic kidney disease in dogs.

Materials and Methods

Criteria for inclusion in Selection of animal: Dogs, irrespective of age, sex, and breed, that were registered at the Veterinary Clinical Complex (VCC), College of Veterinary Science, Khanapara, from different parts of Assam and neighboring states of the North Eastern Region during the period from 1st October 2022 to 30th June 2023, were considered for the study. Dogs with a clinical history and clinical signs suggestive of the disease (such as inappetence, vomiting, oliguria/anuria/polyuria, polydipsia, anemia, weight loss, lethargy, diarrhea and oral manifestations) were screened and subjected to thorough physical examinations, hematological evaluations, serum biochemical profiling, ultrasonography, and urine analysis to confirm the diagnosis of CKD. Details on clinical findings are presented on Table 1

Collection of sample: Blood samples were collected from CKD-suspected dogs on the 0th day (pre-treatment) for the estimation of various haemato-biochemical parameters. Using the venipuncture method, 2 mL of blood was collected aseptically into a K_2-EDTA vial and 3 mL into a clot activator-coated Vacutainer tube. Additionally, approximately 20-25 mL of urine was collected aseptically from suspected CKD dogs in a sterile vial by catheterization, using an infant feeding tube of appropriate size, for routine examination (RE).

Evaluation of haematological parameters

Haematological parameters were evaluated using an Automated Haematology Analyzer (Model MS4Se, MELET SCHLOESING Laboratories). The parameters assessed included white blood cell (WBC) count (m/mm³), red blood cell (RBC) count (M/mm³), hematocrit (Hct) (%), and hemoglobin (Hb) (g/dL)

Evaluation of serum biochemical parameters: Serum biochemical parameters were evaluated using a Clinical Serum Biochemistry Auto-analyzer (Idexx Catalyst One). The parameters assessed included creatinine (mg/dL), blood urea nitrogen (BUN) (mg/dL), total protein (g/dL), albumin (g/dL), phosphorus (mg/dL), calcium (Ca) (mg/dL), potassium (K) (mmol/L), sodium (Na) (mmol/L), and chloride (Cl) (mmol/L).

Urine Analysis: The urine samples were analyzed using Nucleus Diagnostics Nuvision urine test strips with the Nuvision urine strip analyzer. The color and clarity were examined grossly. The parameters evaluated included color, pH, urine specific gravity (USG), urine protein (mg/dL), urine creatinine (mg/dL), and microscopic examination.
Urine protein and creatinine (UPC) ratio was calculated using the following formulas

$$\text{Urine protein and creatinine (UPC) ratio} = \frac{\text{Urinary Total protein (mg/dl)}}{\text{Urinary creatinine (mg/dl)}}$$

Ultrasonography: A color Doppler ultrasound machine (ACUSON NX3 Elite, Siemens Healthineers) was used to perform abdominal ultrasonography to study the architectural changes of the kidneys in dogs with CKD for the present research investigation. A 5-8 MHz convex probe and a 3.5-10 MHz linear probe were utilized.

Staging of CKD: The International Renal Interest Society (IRIS) proposed a classification scheme for CKD based on the use of plasma creatinine concentration in an euvolemic (normally hydrated) animal to estimate the degree of decline in glomerular filtration rate caused by CKD. In the present study, staging was performed to facilitate appropriate patient monitoring and therapy. Table 3. Presents the staging criteria.

Table 1: Staging of CKD

Stage	Description	Serum creatinine level
I	Non-azotaemic CKD	< 1.4mg/dL
II	Mild renal azotaemia	1.4-2.0mg/dL
III	Moderate renal azotaemia	2.1-5.0 mg/dL
IV	Severe renal azotaemia	> 5.0mg/dL

Grouping of dogs to evaluate comparative therapeutical efficacy: A total of 40 dogs, irrespective of age, breed, and sex, found to be affected with CKD were randomly divided into two groups (A and B), comprising 20 dogs in each group, to carry out a therapeutic trial of two different groups of drugs. Additionally, twenty apparently healthy dogs were selected as the control group (Group C) to obtain normal baseline data for comparison of various parameters under study (haemato-biochemical, urine analysis, and nephrosonography). Table 3 presents the treatment groups along with their respective treatment regimens

Table 2: Treatment group with therapeutic regime

Groups	Treatment		
	Drug	**Dose**	**Route**
A	Serum anguillae 6X[1] Urea pura 30 CH[2]	@1 drop in 1 tsf water BID @ 1 drop in 1 tsf water BID	Orally
B	Conventional treatment with Kidney cleanser and kidney symbiotics		
NB: supportive therapy like fluid, antibiotic and multivitamins were given to both the groups			

Table 3: Breed-wise prevalence of CKD in dogs

Breed	Total no. of dogs registered	No. of affected dogs	Prevalence (%)
Labrador Retriever	745	20	0.64
Crossbred	570	4	0.12
German Shepherd	562	4	0.12
Mongrel	652	3	0.09
Golden Retriever	254	5	0.16
German Spitz	310	2	0.06
Pit Bull	62	1	0.03
Great Dane	25	1	0.03
Total	3180	40	1.25

Table 4: Sex-wise prevalence of CKD in dogs

Sex	Total no. of dogs registered	No. of affected dogs	Prevalence (%)
Male	1792	27	1.84
Female	1388	13	0.41
Total	3180	40	1.25

Table 5: Age-wise prevalence of CKD in dogs

Age (years)	Total No. of dogs registered	No. of affected dogs	Prevalence (%)
≤1	1140	0	0
>1-3	920	3	0.09
>3-6	495	10	0.31
>6-10	415	23	0.72
>10	210	4	0.13
Total	3180	40	1.25

Table 6: Clinical signs exhibited by CKD dogs

Clinical signs	No. of affected dogs	Percentage (%)
Inappetance	27	67.50
Oral manifestation	21	52.50
Vomition	20	50.00
Polyuria	19	47.50
Polydipsia	17	42.50
Diarrhoea	14	35.00
Pale mucosal membrane	11	27.50
Congested mucosal membrane	9	22.50
Dehydration	11	27.50
Lethargy	11	27.50
Weight loss	6	15.00
Fever (>102.5˚)	5	12.50
Hematuria	1	2.50

Table 7: Prominent oral manifestation in CKD dogs

Oral manifestation	No. of affected dogs	Percentage (%)
Halitosis	10	47.62
Dental tartar	5	23.80
Dental caries	3	14.29
Oral ulcer	3	14.29
Total	21	100.00

Table 8: Mean ± SE of haematology pre-and post-treatment days

Parameters	Group A					Group B					Group C				
	Pre-treatment	Post- treatment				Pre-treatment	Post -treatment				Pre-treatment	Post -treatment			
	0th	7th	14th	21st	28th	0th	7th	14th	21st	28th	0th	7th	14th	21st	28th
RBCs (10^6/µl)	$6.08\pm0.36^{A}_{a}$	$6.41\pm0.28^{A}_{ab}$	$7.29\pm0.34^{A}_{c}$	$6.69\pm0.22^{A}_{abc}$	$7.02\pm0.23^{A}_{bc}$	$6.05\pm0.40^{A}_{a}$	$6.10\pm0.34^{A}_{ab}$	$6.84\pm0.32^{A}_{bc}$	$7.20\pm0.39^{A}_{c}$	$7.04\pm0.21^{A}_{c}$	$6.67\pm0.20^{A}_{a}$	$6.60\pm0.20^{A}_{a}$	$7.06\pm0.17^{A}_{a}$	$7.03\pm0.16^{A}_{a}$	$7.17\pm0.15^{A}_{a}$
WBC (10^3/µl)	$25.87\pm5.57^{A}_{a}$	$18.20\pm1.64^{AB}_{b}$	$15.23\pm0.76^{A}_{c}$	$13.47\pm0.69^{A}_{c}$	$12.12\pm0.58^{A}_{c}$	$22.57\pm3.59^{A}_{a}$	$20.17\pm2.38^{A}_{ab}$	$14.23\pm0.92^{A}_{bc}$	$13.44\pm0.59^{A}_{c}$	$12.24\pm0.48^{A}_{c}$	$22.57\pm3.59^{A}_{a}$	$20.17\pm2.38^{A}_{ab}$	$14.23\pm0.92^{A}_{bc}$	$13.44\pm0.59^{A}_{c}$	$12.24\pm0.48^{A}_{c}$
Hct (%)	$35.61\pm1.57_{ab}$	$38.59\pm1.48_{bc}$	$43.69\pm1.92_{cd}$	$41.90\pm1.46_{cd}$	$45.52\pm1.83_{d}$	$37.87\pm2.77_{a}$	$39.81\pm3.06_{ab}$	$42.33\pm1.74_{abc}$	$44.27\pm1.83_{bc}$	$46.42\pm1.86_{c}$	$41.57\pm1.63_{a}$	$41.85\pm1.43_{a}$	$41.58\pm1.18_{a}$	$42.70\pm1.22_{a}$	$45.67\pm1.19_{a}$
Hb(g/dL)	11.13±0.63	12.45±0.54	15.71±2.45	13.08±0.40	13.14±0.46	11.35±0.72	12.43±0.79	15.08±2.64	12.77±0.48	12.62±0.34	12.14±0.49	13.13±0.31	12.87±0.37	13.62±0.35	13.25±0.34
NB: Means with different superscripts (A,B,C) within column and subscripts (a,b,c) within row differ significantly (P<0.05).															

Table 9: Mean±SE of serum biochistry pre-and post-treatment days

Parameters	Group A					Group B				Group C					
	Pre-treatment	Post- treatment				Pre-treatment	Post -treatment			Pre-treatment	Post -treatment				
	0th	7th	14th	21st	28th	0th	7th	14th	21st	28th	0th	7th	14th	21st	28th
Creatinine (mg/dL)	$5.39\pm0.95^{A}_{a}$	$3.90\pm0.96^{A}_{a}$	$2.26\pm0.57^{A}_{b}$	$1.34\pm0.05^{A}_{b}$	$1.28\pm0.05^{A}_{b}$	$4.88\pm0.78^{A}_{a}$	$4.10\pm0.98^{A}_{a}$	$1.65\pm0.09^{B}_{b}$	$1.52\pm0.06^{A}_{b}$	$1.35\pm0.05^{A}_{b}$	$1.15\pm0.04^{B}_{a}$	$1.19\pm0.04^{B}_{a}$	$1.22\pm0.03^{B}_{a}$	$1.22\pm0.03^{A}_{a}$	$1.23\pm0.04^{A}_{a}$
BUN (mg/dL)	$66.90\pm8.30^{A}_{a}$	$53.44\pm8.80^{A}_{a}$	$33.86\pm4.83^{A}_{b}$	$23.42\pm1.08^{A}_{b}$	$21.75\pm0.93^{A}_{b}$	$54.45\pm6.83^{A}_{b}$	$46.89\pm9.00^{A}_{b}$	$21.69\pm1.63^{BA}_{b}$	$19.62\pm1.61^{A}_{b}$	$16.10\pm0.95^{B}_{b}$	$15.90\pm0.95^{B}_{b}$	$17.25\pm1.03^{B}_{b}$	$17.40\pm0.99^{A}_{b}$	$17.35\pm0.93^{A}_{b}$	$16.10\pm0.95^{B}_{b}$
Total Protein (g/dL)	7.82±0.38	7.33±0.39	7.34±0.38	6.82±0.24	6.82±0.24	7.88±0.32	7.73±0.32	6.94±0.21	7.18±0.20A	6.94±0.13	7.14±0.12	6.90±0.18	7.28±0.21	7.13±0.17	7.03±0.23
Albumin (g/dL)	$1.56\pm0.70^{A}_{a}$	$1.79\pm0.05^{A}_{b}$	$1.87\pm0.08^{A}_{b}$	$2.12\pm0.09^{A}_{c}$	$2.43\pm0.08^{A}_{d}$	$1.35\pm0.07^{B}_{a}$	$1.57\pm0.07^{B}_{b}$	$1.75\pm0.06^{A}_{c}$	$1.97\pm0.06^{A}_{d}$	$2.31\pm0.05^{A}_{e}$	$2.84\pm0.07^{C}_{a}$	$2.19\pm0.05^{C}_{a}$	$2.90\pm0.05^{B}_{a}$	$2.96\pm0.05^{B}_{a}$	$2.97\pm0.09^{B}_{a}$
PHOSPHORUS (mg/dL)	$7.11\pm1.07^{A}_{a}$	$7.31\pm1.25^{A}_{a}$	$6.79\pm1.22^{A}_{a}$	$4.78\pm0.22^{A}_{b}$	$4.65\pm0.22^{A}_{b}$	$7.29\pm1.15^{A}_{a}$	$6.56\pm0.77^{AB}_{a}$	$4.96\pm0.32^{AB}_{b}$	$4.91\pm0.30^{A}_{b}$	$4.76\pm0.29^{A}_{b}$	$4.68\pm0.20^{B}_{a}$	$4.64\pm0.20^{B}_{a}$	$4.73\pm0.17^{B}_{a}$	$4.69\pm0.17^{A}_{a}$	$4.71\pm0.16^{A}_{a}$
CALCIUM (mg/dL)	9.18±0.20	9.15±0.20	9.33±0.21	9.55±0.18	9.57±0.19	9.15±0.25	9.32±0.27	9.69±0.26	9.73±0.25	9.73±0.24	9.53±0.21	9.65±0.25	9.63±0.22	9.60±0.19	9.66±0.22
POTASSIUM (mmol/L)	$5.15\pm0.25^{A}_{a}$	$4.99\pm0.28^{AB}_{a}$	$4.83\pm0.22^{AB}_{a}$	$4.71\pm0.19^{A}_{a}$	$4.63\pm0.16^{A}_{a}$	$5.50\pm0.35^{A}_{a}$	$5.19\pm0.24^{A}_{ab}$	$5.19\pm0.42^{A}_{ab}$	$4.66\pm0.15^{A}_{b}$	$4.62\pm0.13^{A}_{b}$	$4.37\pm0.21^{B}_{a}$	$4.42\pm0.18^{B}_{a}$	$4.49\pm0.18^{B}_{a}$	$4.39\pm0.18^{A}_{a}$	$4.38\pm0.17^{A}_{a}$
SODIUM (mmol/L)	$147.85\pm0.92_{a}$	$149.83\pm1.01_{a}$	$151.00\pm0.65_{b}$	$151.23\pm0.87_{b}$	$151.62\pm0.93_{b}$	$148.40\pm1.40_{a}$	$150.67\pm1.12_{ab}$	$151.64\pm0.75_{bc}$	$152.31\pm0.69_{c}$	$152.62\pm0.79_{c}$	$149.75\pm0.89_{a}$	$150.65\pm0.98_{ab}$	$150.75\pm0.48_{ab}$	$151.45\pm0.62_{b}$	$151.95\pm0.73_{b}$
CHLORIDE (mmol/L)	$109.90\pm1.71^{A}_{a}$	$110.72\pm1.38^{A}_{ab}$	$110.87\pm1.48^{A}_{ab}$	$113.31\pm0.80^{A}_{b}$	$113.77\pm0.61^{A}_{b}$	$108.85\pm1.64^{A}_{a}$	$111.17\pm1.16^{A}_{ab}$	$112.43\pm1.08^{A}_{bc}$	$114.54\pm0.92^{A}_{c}$	$115.08\pm0.73^{A}_{c}$	$114.00\pm0.92^{B}_{a}$	$113.05\pm1.15^{A}_{a}$	$113.40\pm0.86^{A}_{a}$	$114.55\pm0.69^{A}_{a}$	$115.15\pm0.60^{A}_{a}$
NB: Means with different superscripts (A,B,C) within column and subscripts (a,b,c) within row differ significantly (P<0.05).															

Table 10: Mean ± SE UPC ratio on pre and post treatment days

Groups	Pre-treatment	Post-treatment	
	0 day	14th day	28th day
A	$1.43\pm1.32^{A}_{a}$	$0.72\pm0.71^{A}_{b}$	$0.52\pm0.78^{A}_{b}$
B	$1.56\pm2.44^{A}_{a}$	$0.92\pm3.08^{A}_{b}$	$0.58\pm1.32^{A}_{b}$
C	$0.02\pm0.32^{B}_{a}$	$0.02\pm0.42^{B}_{a}$	$0.02\pm0.55^{B}_{a}$
NB: Means with different superscripts (A,B,C) within column and subscripts (a,b,c) within row differ significantly ($P<0.05$).			

Table 11: Staging of CKD dogs according to iris standard

Serum Creatinine level	CKD Stage	No. of dogs	Percentage (%)
< 1.4mg/dL	I	0	0
1.4-2.0mg/dL	II	10	25
2.1-5.0 mg/dL	III	14	35
> 5.0mg/dL	IV	16	40
Total		40	100

Data analysis: Statistical analysis of the experimental data was carried out using two-way ANOVA (SAS Enterprise Guide 9.3 version).

Result:

In the present study, out of 3,180 dogs registered at the VCC, 40 cases of CKD were confirmed, yielding a prevalence rate of 1.25% (Fig 1). The highest prevalence was observed in Labrador Retrievers (0.64%) (Fig 2), with males (0.84%) more frequently affected than females (0.41%) (Fig 3). CKD was most common in dogs aged >6-10 years (0.72%), followed by those aged >3-6 years (0.31%), >10 years (0.13%), and >1-3 years (0.09%) (Fig 4). No cases were recorded in dogs younger than 1 year.

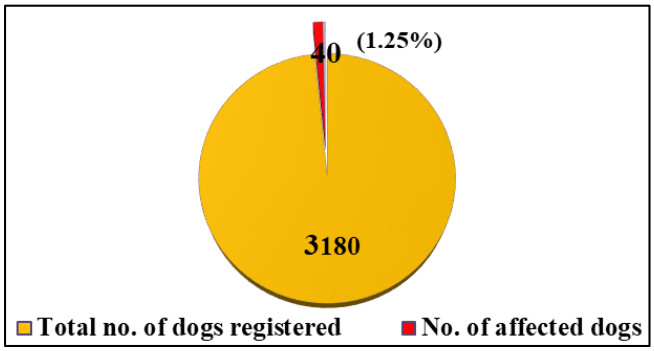

Fig 1: Pie diagram showing prevalence of CKD in dogs

Fig 2: Cachexia

Fig 3: Hematuria

Fig 4: Bloody vomitus

Clinical signs: The most prominent clinical signs observed during the study were inappetence (67.5%), followed by oral manifestations (52.5%), vomiting (50%), polyuria (47.5%), polydipsia (42.5%), diarrhoea (35%), pale mucous membranes (27.5%), congested mucous membranes (22.5%), dehydration (27.5%), lethargy (27.5%), weight loss (15%), fever (12.5%), and haematuria (2.5%) (Fig 5).

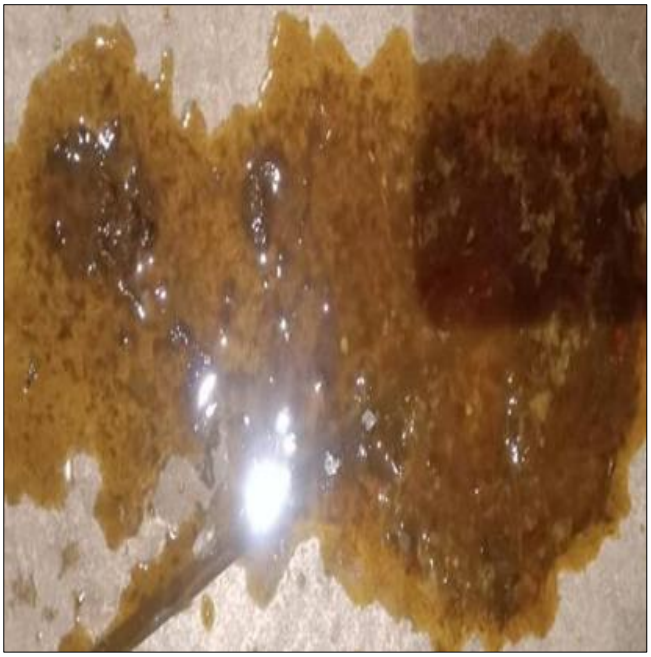

Fig 5: Bilious vomitus

Haemato-biochemical evaluation: Haemato-biochemical assessment revealed a significant increase in WBC count, serum creatinine, BUN, phosphorus, and potassium levels, along with a decrease in serum albumin and chloride levels in both CKD-affected groups (A and B) compared to the apparently healthy group C. The serum levels of total protein, calcium, and sodium remained within the normal range throughout the study period. (Fig 6)

Fig 6: Oral ulcer (red arrow), dental caries (yellow arrow)

Urine analysis: Urine routine examination (RE) of CKD-positive dogs revealed amber to deep amber-colored urine with an overall pH of 6.8. An isosthenuric urine specific gravity was observed, along with a significant (P<0.01) increase in urine protein levels, urine protein-to-creatinine ratio, and the presence of cells, casts, and crystals (Fig 7).
Nephrosonographic examination revealed that the majority of CKD-affected dogs exhibited hyperechoic and thickened renal cortices, partial or complete loss of cortico-medullary differentiation, and a wavy capsule. (Fig 8)

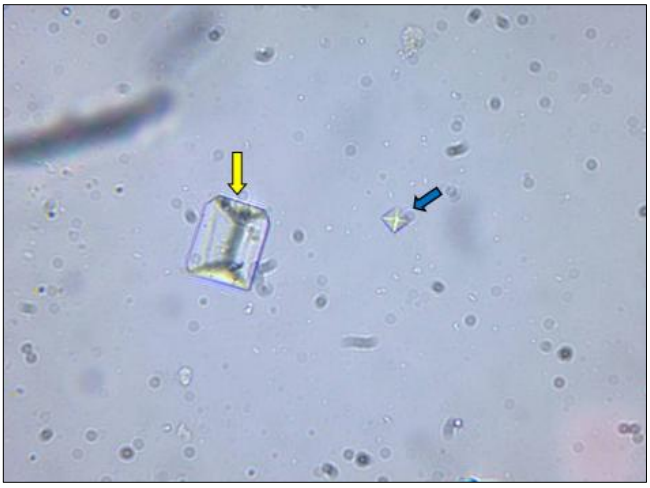

Fig 7: Triple phosphate (Yellow arrow) and calcium oxalate (blue arrow) (40X)

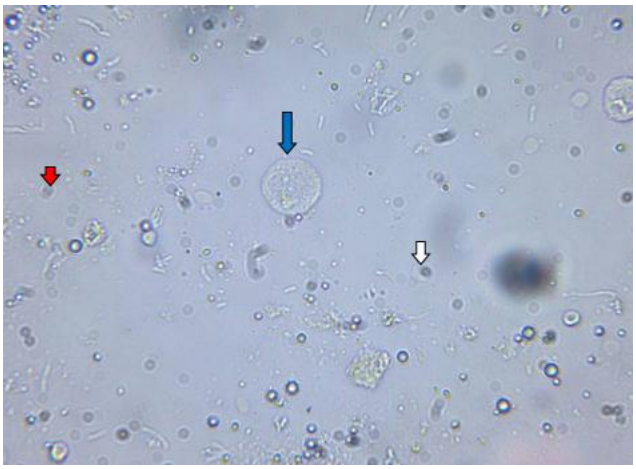

Fig 8: Epithelial cells (blue arrow), RBC (red arrow) and WBC (white arrow) (40X)

Comparative evaluation of treatment regimen: CKD-affected dogs in stages II, III, and IV were randomly divided for two different therapeutic management studies. Group A received serum anguillae and urea pura (Homeopathy) with supportive therapy, while Group B was treated with a kidney cleanser, symbiotic, and supportive care. Significant improvement was observed in stage II and III dogs in both groups (Fig 9). However, all stage IV dogs failed to respond and died despite intensive treatment efforts.

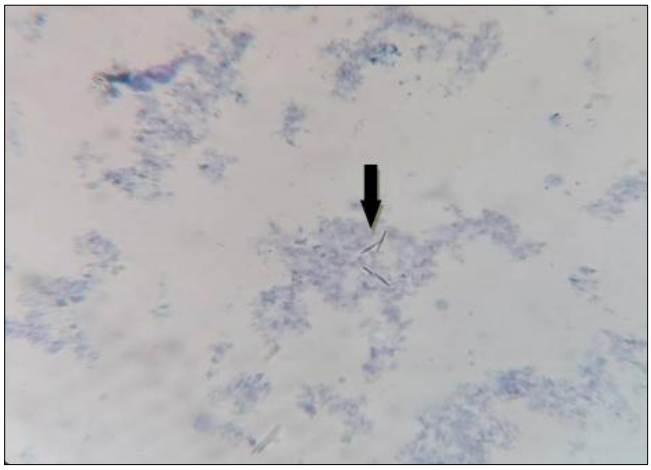

Fig 9: Uric acid crystal stained with methylene blue (40x)

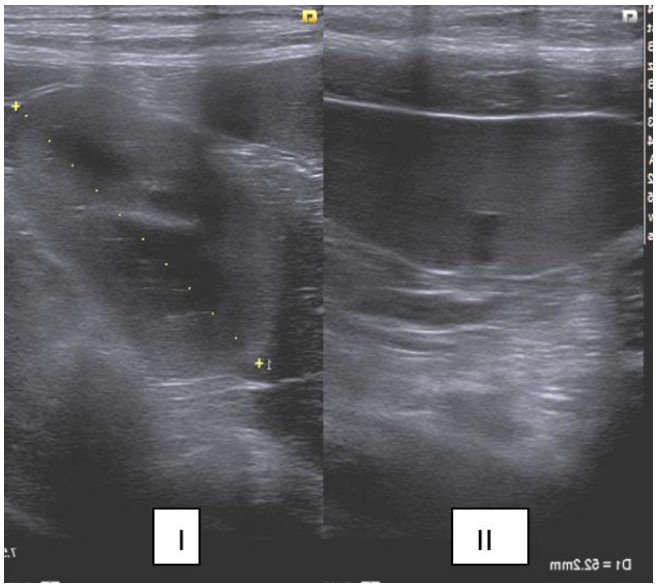

Fig 10: Comparision of cortical echogenicity of kidney (I) with spleen parenchyma (II)

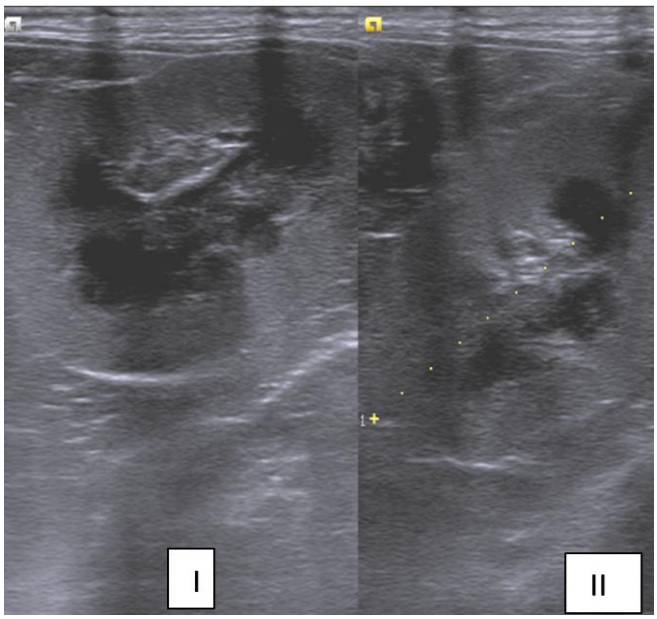

Fig 11: Comparision of rt. kidney (I) and lt. kidney (II) both having hyperechoic thick cortex with partial loss of CMD and irregular capsule in lt kidney

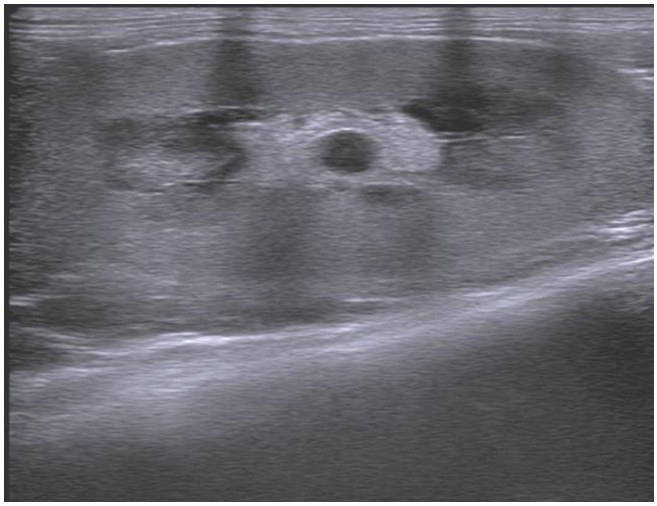

Fig 12: Hyperechoic thickened cortex with loss of CMD, wavy capsule and dilated pelvis

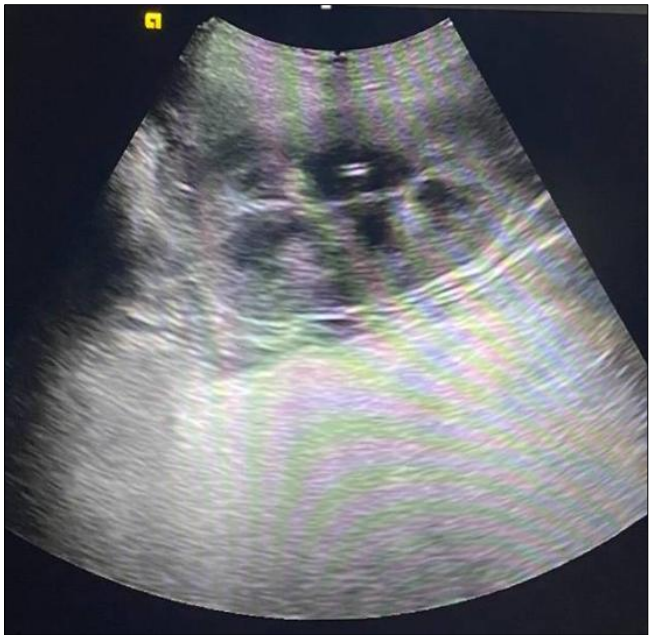

Fig 13: Kidney showing hyperechoic cortex with hazyness of the CMD and wavy capsule

Discussion

In the present study, the prevalence rate of chronic kidney disease (CKD) recorded during the present study was 1.25%. This finding differed from the reports of Tufani *et al.* (2015) [41] and Karunanithy *et al.* (2019) [20], who observed higher prevalence rates of 2.58% and 2.22%, respectively. The variation in prevalence may be attributed to differences in the method of calculation, population size, duration of study and screening period. Among the different breeds reported in the present study, Labrador Retriever was the most affected breed (0.64%), which is in agreement with the findings of Tufani *et al.* (2015) [41] and Joshi *et al.* (2021). Regarding sex-wise prevalence, male dogs (0.84%) exhibited a higher prevalence rate of CKD than female dogs (0.41%), similar to the observations of Katoch *et al.* (2017) [21], Athaley (2018) [1] and Meena *et al.* (2022) [26]. A higher prevalence in male dogs may be attributed to an increased risk of urolithiasis due to certain anatomical characteristics and various prostate disorders, wherein an enlarged prostate can obstruct the normal flow of urine (Katoch *et al.*, 2017; Kumar *et al.*, 2020b) [21, 22]. Age-wise prevalence revealed a higher occurrence in the age group >6-10 years (0.72%). These findings are in agreement with those of Katoch *et al.* (2017) [21], Devipriya *et al.* (2018) and Reddy *et al.* (2021). The most prominent clinical signs observed during the study were inappetence (67.5%), followed by oral manifestations (52.5%), vomiting (50%), polyuria (47.5%), polydipsia (42.5%), diarrhoea (35%), pale mucous membranes (27.5%), congested mucous membranes (22.5%), dehydration (27.5%), lethargy (27.5%), weight loss (15%), fever (12.5%) and haematuria (2.5%). These observations were similar to earlier studies conducted by different workers (Chew *et al.*, 2011; Foster, 2013; Nakang, 2017; Tufani *et al.*, 2017; Kumar *et al.*, 2020a; Sheeran, 2021) [6, 28, 42, 37, 22].

A significant ($P<0.01$) increase in WBC count was observed in both CKD-affected Groups A and B compared to the healthy control Group C. These findings were in agreement with earlier reports by Sumit *et al.* (2018) [39], Sonu *et al.* (2019) [38] and Gupta *et al.* (2022) [15]. The

Mean±SE values of RBC, Hb, and Hct in both CKD-affected groups remained within the normal range, similar to the healthy controls, corroborating the findings of Borin-Crivellenti *et al*. (2014) [4].

A significant (P<0.01) increase in serum creatinine and BUN levels was recorded in Groups A and B when compared with the healthy control group. These results were consistent with previous observations by Nakang (2017) [28], Sumit *et al*. (2018) [39] and Kalyani *et al*. (2022) [18]. In Group A, CKD-affected dogs were treated with homeopathic medicines *Serum anguillae* and *Urea pura*, which work on the principle of "like cures like" (Boericke, 2008) [3]. This principle suggests that administration of such a medicine creates a stronger medicinal disease, which eventually subsides, allowing the vital force to overcome both natural and medicinal diseases and restore health (Das, 2001) [10].

Serum anguillae, derived from eel fish, exerts an elective effect on the kidneys. Eels adapt to both hypertonic and hypotonic environments during metamorphosis, which might explain the medicine's supportive effect on diseased kidneys (Choudhary, 2017; Bodkhe, 2021) [7, 2]. However, further investigations are necessary to validate this hypothesis.

In Group B, CKD-affected dogs were treated conventionally with Kidney Cleanser (Rkleen) and Kidney Symbiotic (Renodyl). *Tribulus terrestris*, an ingredient of Rkleen, promotes diuresis by increasing GFR, thus aiding in the detoxification of kidneys. Renodyl helps by metabolizing uremic toxins into nutrients, thereby reducing toxin accumulation and preventing further renal damage.

The serum total protein levels in CKD-affected dogs (Groups A and B) remained within the normal range and were comparable to healthy controls. However, serum albumin levels were significantly (P<0.05) lower in both CKD-affected groups compared to the healthy controls, aligning with the findings of Oburai *et al*. (2015) and Nakang (2017) [28].

A significant (P<0.05) increase in serum phosphorus levels was noted in CKD-affected dogs compared to healthy controls, similar to findings reported by Sumit *et al*. (2018) [39], Vervloet *et al*. (2018) [43], Ribeiro *et al*. (2020) [35], and Thade *et al*. (2021) [40]. No significant difference (P>0.01) in serum calcium levels was observed among the groups, corroborating the findings of Ribeiro *et al*. (2020) [35].

A significant (P<0.05) increase in serum potassium levels was observed in CKD-affected groups compared to healthy controls, consistent with the observations of Kumar *et al*. (2011) [23] and Sumit *et al*. (2018) [39]. A non-significant (P>0.01) reduction in serum sodium levels and a significant (P<0.05) reduction in serum chloride levels were also recorded, aligning with the findings of Thade *et al*. (2021) [40].

Urinalysis revealed that the urine colour in CKD-affected dogs varied from amber to deep amber, while healthy dogs showed pale yellow or transparent urine. The urine pH remained within the normal range in all groups, which was similar to the observations by Kennedy *et al*., and Kaneko *et al*. (2008). A highly significant (P<0.01) increase in urine protein levels was recorded in CKD-affected groups, comparable with findings by Grauer (2007) [14] and Harley *et al*. (2012) [47].

Persistent proteinuria with a mean UPC (Urine Protein to Creatinine Ratio) of 1.49±1.61 was recorded in CKD-affected dogs, indicating the presence of tubular proteinuria and glomerulonephritis, consistent with Jacob *et al*. (2005) [48]. Such conditions may increase the risk of uremic morbidity and mortality in CKD-affected dogs.

The majority of CKD-affected cases were recorded in Stage III (35.00%) and Stage IV (37.50%), with no cases found in Stage I. These findings were similar to those reported by Polzin (2013) [33] and Nakang (2019) [28]. The absence of Stage I cases might be attributed to the fact that serum creatinine concentrations in Stage II often fall within the normal reference range for many laboratories, making early detection difficult (Grauer, 2017) [14].

In the present study, the majority of the CKD-affected dogs exhibited hyperechoic and thickened renal cortices (100.00%), along with partial loss (23.00%) or complete loss (42.50%) of cortico-medullary differentiation (CMD) and a wavy capsule (37.50%). These findings were in agreement with the observations of Bragato *et al*. (2017) and Kumar *et al*. (2020c) [22], who reported that increased cortical echogenicity might be attributed to glomerulosclerosis and fibrotic changes occurring in the diseased kidneys.

Comparative therapeutic management of CKD in dogs

The present study focused on evaluating cost-effective therapeutic alternatives to conventional treatment for CKD in dogs, using two different branches of complementary and alternative medicine. The efficacy of the treatment regimens was assessed based on improvements in haemato-biochemical parameters, clinical recovery, urine RE, and ultrasonography findings over a 28-day period at weekly intervals. Haematological parameters (WBC, RBC, Hct, and Hb) showed significant improvement in both treatment groups (A and B). Biochemical markers related to kidney function serum creatinine, BUN, albumin, phosphorus, potassium, and chloride also improved significantly by the end of the study, while total protein, calcium, and sodium levels remained within normal limits. Clinical signs and symptoms reduced markedly in both groups within weeks, indicating comparable therapeutic efficacy.

Based on the findings, it was concluded that homeopathic treatment with *Serum anguillae* 6X and *Urea pura* 30CH, along with supportive therapy, showed promising results in slowing disease progression and improving the overall condition of CKD-affected dogs, comparable to conventional treatment. It was found that in Group A, dogs undergoing homeopathic treatment along with supportive therapies at IRIS stages I, II, and III survived throughout the study period without complications. Homeopathy is considered safe, with no reported side effects or allergies (Loken, 2001; Mathie *et al*., 2007; Chavelikar *et al*., 2016; Jaguezeski *et al*., 2021; Weiermayer *et al*., 2022) [5]. Similarly, in Group B, conventional treatment combined with supportive therapy showed 100% survival in CKD stages II and III.

However, in both groups, all dogs with IRIS stage IV CKD succumbed despite intensive therapeutic management. These findings align with previous studies (Roudbush *et al*., 2010; Polzin, 2013; Nakang, 2017; O'Neill *et al*., 2013; Rudinsky *et al*., 2018) [36, 33, 28], which reported significantly higher mortality risks in dogs at IRIS stages III and IV. Medical management of CKD primarily aims to minimize clinical and pathophysiological consequences, rather than reversing renal damage (Roudbush *et al*., 2010) [36].

The present study contributes to understanding the mechanisms involved in the progression of different stages of chronic kidney disease (CKD). It also highlights the

potential role of homeopathic medicine as an effective and safe adjunct therapy. Several studies in both human and veterinary medicine have demonstrated the benefits of homeopathic treatments, emphasizing their therapeutic significance. Based on the findings of this study, homeopathic medicine appears to be a promising, cost-effective alternative or complementary approach for managing chronic diseases such as CKD.

However, further extensive, controlled clinical studies are needed to validate these findings, establish standardized treatment protocols, and better elucidate the mechanisms by which homeopathic therapies exert their effects. Future research focusing on large-scale trials and long-term outcomes would help reinforce the scientific basis for integrating homeopathic medicine into mainstream veterinary practice

Conflict of interest: Authors have no conflict of interest in this study

Author's contribution

Data availability statement: The data used to support the findings of this study are included within the article

Ethical Statement

This study did not require ethical approval, as all blood samples were collected from suspected cases solely for diagnostic purposes. All animals were handled humanely using non-invasive methods, and all procedures were conducted in compliance with the ethical standards of the institution where the study was performed.

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