P-ISSN: 2304-3075; E-ISSN: 2305-4360
International Journal of Veterinary Science
www.ijvets.com; editor@ijvets.com

Research Article https://doi.org/10.47278/journal.ijvs/2025.101

Exploring the Therapeutic Potential of Mesenchymal Stem Cells-Derived Secretome in Cats with Kidney Disease

Guntari Titik Mulyani [1], Yuda Heru Fibrianto [2] and Teguh Budipitojo [3,*]

[1]Department of Internal Medicine, Faculty of Veterinary Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia
[2]Department of Physiology, Faculty of Veterinary Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia
[3]Department of Anatomy, Faculty of Veterinary Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia
***Corresponding author:** budipitojo@ugm.ac.id

Article History: 25-138 Received: 28-May-25 Revised: 17-Jul-25 Accepted: 24-Jul-25 Online First: 17-Sep-25

ABSTRACT

Feline kidney disease, including acute kidney injury (AKI) and chronic kidney disease (CKD), represents a significant clinical challenge due to its high prevalence and limited response to conventional therapies. This study explored the potential benefits of secretome derived from human umbilical cord mesenchymal stem cells (hUC-MSCs), which represents a novel and cell-free regenerative therapeutic approach. Ten domestic cats diagnosed with AKI or CKD were treated with weekly intramuscular injections of hUC-MSC-derived secretome at a dosage of 0.2mL/kg for eight weeks. Clinical evaluations consist of physical examinations, hematologic and biochemical profiling, urinalysis, and renal ultrasonography. The intervention led to notable improvements in appetite, hydration, hematologic parameters, and reductions in blood urea nitrogen (BUN) and creatinine concentrations. In addition, sonographic assessments revealed enhancements in renal morphology, especially among cats with AKI. These findings suggest that hUC-MSC-derived secretome holds promise as an adjunctive therapeutic modality for feline kidney disease. Further controlled studies are essential to substantiate these preliminary observations.

Key words: Acute kidney injury, Chronic kidney disease, Felines, Regenerative medicine, Secretome

INTRODUCTION

Kidney disorders represent a significant clinical concern in small animal practice, especially among aging cats and male individuals. Acute kidney injury (AKI) often arises from various etiologies, including ischemic events, inflammatory processes, exposure to nephrotoxins, or infectious agents such as *Leptospira*, which has been associated with interstitial nephritis and tubular necrosis (Bartges 2012; Bezerra et al. 2018; Segev et al. 2024). Unlike AKI, chronic kidney disease (CKD) is characterized by progressive, irreversible loss of renal function that persists beyond three months. This condition typically becomes clinically evident only after substantial nephron damage—exceeding 75%—has occurred (Harvey and Bruss 2021; Griffith and Johnson 2022). Both AKI and CKD can contribute significantly to morbidity and mortality in feline patients, with CKD being one of the primary causes of death in geriatric cats. Prevalence estimates vary but may reach up to 20% in certain populations (Lund et al. 1999; Polzin 2010; O'Neill et al. 2015). The pathogenesis of CKD is multifactorial and includes influences such as age, breed predisposition, hypertension, proteinuria, incomplete recovery from prior AKI episodes and other systemic or metabolic contributors (Hasegawa et al. 2017).

Despite advances in supportive care, current therapeutic approaches for feline kidney disease remain largely palliative. Conventional treatments—such as fluid resuscitation, diuretics (e.g., furosemide, dopamine), gastroprotective agents, phosphate binders, antiemetics, antioxidants, bicarbonate supplementation for metabolic acidosis, and antibiotic therapy—are often insufficient for halting disease progression, especially in the absence of renal replacement options like dialysis or transplantation (Ross 2014, Harel et al. 2014). These latter interventions are rarely feasible in routine veterinary settings due to logistical, economic and ethical constraints.

Against this backdrop, regenerative medicine has emerged as a potential avenue for enhancing renal recovery. Among the most studied candidates are mesenchymal stem cells (MSCs), which offer several biological advantages including multipotency, self-renewal capability, immunomodulation and the ability to differentiate into

Cite This Article as: Mulyani GT, Fibrianto YH and Budipitojo T, 2026. Exploring the therapeutic potential of mesenchymal stem Cells-derived secretome in cats with kidney disease. International Journal of Veterinary Science 15(1): 34-40. https://doi.org/10.47278/journal.ijvs/2025.101

renal tubular epithelial cells (Ilic and Ogilvie 2017; Han et al. 2021; Broekema et al. 2005). Notably, the therapeutic effects of MSCs are increasingly attributed not only to direct cellular integration but also to their secretory profile, referred to as the secretome.

The MSC secretome consists of a complex mixture of soluble molecules, such as growth factors, cytokines, hormones and lipid mediators, that together create a microenvironment suitable for cellular regeneration (Ranganath et al. 2012). These paracrine factors have shown promise in promoting tissue repair and modulating inflammation in a variety of organ systems, including the kidneys. Compared to cell-based transplantation, secretome therapy offers several advantages. It poses minimal immunogenic risk, is easier to store and administer, and eliminates concerns related to uncontrolled cell proliferation. In a canine model, Seung et al. (2017) demonstrated that secretome derived from umbilical cord MSCs improved renal function by reducing serum blood urea nitrogen (BUN) and creatinine levels. The regenerative potential of secretome therapy is attributed to its ability to inhibit apoptosis, reduce fibrosis, and activate endogenous repair mechanisms (Chen et al. 2008).

Given the limited research on the use of MSC-derived secretome in clinical veterinary nephrology—particularly in feline patients—this study aimed to evaluate its therapeutic potential in cats diagnosed with AKI or CKD. The investigation was designed to assess clinical, hematological, biochemical and ultrasonographic parameters before and after secretome administration

MATERIALS AND METHODS

This prospective, observational study enrolled ten domestic cats that were presented to veterinary clinics in Yogyakarta, Indonesia, showing clinical indications of renal dysfunction. Prior to inclusion, owners provided informed consent, and the protocol was approved by the Animal Ethics Committee of Universitas Gadjah Mada.

Kidney disease was diagnosed through an integrative approach combining physical examination, blood chemistry, urinalysis and ultrasonographic findings. Cases classified as acute kidney injury (AKI) were characterized by a sudden onset of dehydration, weak pulse, muscle tremors, and asymmetrical renal dimensions observed via ultrasonography. Chronic kidney disease (CKD) was identified in cats that had persistent polyuria, polydipsia, weight loss, muscle wasting, and sonographic evidence of bilaterally small kidneys with reduced corticomedullary distinction (Jepson et al. 2009; Larry et al. 2016; Rimer et al. 2022).

Laboratory assessment included serum creatinine, blood urea nitrogen (BUN), red and white blood cell counts, packed cell volume (PCV), and hemoglobin levels. Urinalysis was conducted to assess specific gravity, protein concentration, pH, color, clarity, and the presence of erythrocytes, leukocytes, or crystals. Ultrasonography was performed using a linear probe to evaluate changes in renal shape, size, echogenicity, and internal structure.

Extraction of secretome

Secretome was extracted from human umbilical cord-derived mesenchymal stem cells (hUC-MSCs), which were expanded under aseptic, GMP-compliant laboratory conditions. Following confluence, cultures were washed with sterile phosphate-buffered saline (PBS) and incubated in serum-free medium to allow for the secretion of biologically active factors. The conditioned medium was then filtered, aliquoted, and stored at –80°C, following a previously modified protocol for stem cell secretome collection (IRIS 2005; Mahmoud 2024).

Treatment protocol

Each cat received intramuscular injections of the prepared secretome once weekly at a dose of 0.2 mL per kilogram of body weight, for a total duration of up to eight weeks or until marked clinical improvement was observed (Prihatno et al. 2018). Injection sites were alternated weekly to reduce the likelihood of localized irritation or tissue reactivity.

Patients were monitored on a weekly basis for clinical status, which included evaluations of appetite, hydration, body weight, and urination frequency. Hematologic and renal parameters were measured using standard laboratory techniques. Urinalysis was repeated at each visit, and renal ultrasound was performed to track morphologic changes in kidney structure. Owing to the pilot nature of the study and the limited number of cases, outcomes were assessed descriptively without statistical testing.

Statistical analysis

Due to the pilot nature of this observational study and the limited sample size, data were analyzed using descriptive methods only. No inferential statistical tests were applied. Numerical values were presented as absolute numbers, means, or percentages where appropriate, and trends over time were illustrated using line graphs. All data were processed and visualized using Microsoft Excel (version 2021).

RESULTS

This study involved ten feline patients diagnosed with varying degrees of renal pathology. Among them, seven were male, and five were classified as domestic breed cats. All individuals were within the young adult age group (1–6 years). Clinical manifestations varied, but the most consistently observed symptom across the sample was reduced appetite. Weight loss was evident in 60% of cases, while vomiting and dehydration were each reported in half of the subjects. Altered urination patterns, such as increased frequency or difficulty in voiding, were also noted. A complete overview of clinical signs is provided in Table 1.

Hematologic analysis revealed that 70% of the cats had decreased red blood cell (RBC) counts, with 50% also presenting with lowered hemoglobin concentrations. Furthermore, 80% exhibited a reduction in packed cell volume (PCV), and leukocyte counts were elevated in 40% of the cases. These findings are summarized in Table 2, along with blood chemistry profiles.

Urinalysis findings indicated a high frequency of proteinuria (90%) and hematuria (90%), while leukocytes were present in the urine of 60% of cats. Struvite crystals were detected in 30% of samples. Other notable urine abnormalities included altered color, turbidity and abnormal specific gravity and pH values. Table 3 shows the full urinalysis profiles.

Table 1: Clinical symptoms in 10 cats with kidney disease

No	Sample	Signalemen	Anorexia	Weight loss	urination disorders	polydipsia	vomit	dehydration
1	Cat 1	Dom,♂, 6 y	yes	yes	polyuria	yes	yes	yes
2	Cat 2	Mixdom,♀, 2 y	yes	yes	polyuria	yes	no	yes
3	Cat 3	Himalaya,♂, 1.5 y	yes	no	polakiuria	yes	no	no
4	Cat 4	Mixdom,♀, 1 y	yes	yes	no	no	yes	no
5	Cat 5	Dom, ♀, 6y	yes	yes	polyuria	no	yes	yes
6	Cat 6	Mixdom, ♂, 6y	yes	no	stranguria	no	yes	no
7	Cat 7	Persia,♂ , 3y	yes	yes	polyuria	yes	yes	yes
8	Cat 8	Dom, ♂, 2 y	yes	no	polakiuria	no	no	no
9	Cat 9	Dom, ♂, 4y	yes	yes	polyuria	no	no	yes
10	Cat 10	Dom, ♂, 2y	yes	no	polakiuris	no	no	yes

Table 2: Hematology and blood chemistry profile of cats with kidney disease

No	Sample	Erythrocytes (10^6/µL)	Haemoglobine (gr/dL)	Hematocryt (%)	Leucocytes (10^3/µL)	BUN (mg/dL)	Creatinine (mg/dL)
Reference interval*		6.0-10.1	9.5-15	29-45	5.5-19.5	15.3-22.8	0.6-1.4
1	Cat 1	3.41	4.90	14.30	12.56	75.00	5.10
2	Cat 2	4.64	6.70	19.30	19.98	126.45	7.00
3	Cat 3	5.90	10.00	26.00	10.15	44.67	2.18
4	Cat 4	6.92	11.30	31.60	18.98	126.45	14.20
5	Cat 5	3.45	5.50	17.10	20.90	101.82	2.92
6	Cat 6	10.83	11.80	33.00	16.65	155.60	4.49
7	Cat 7	2.44	3.50	12.30	19.01	127.00	5.70
8	Cat 8	5.84	12.00	27.00	27.10	86.83	5.83
9	Cat 9	2.69	2.50	7.20	51.71	63.00	2.70
10	Cat 10	6.80	12.40	25.00	23.25	95.93	3.50

*Reference: (20). Note: Bold print has changed from the normal standard.

Table 3: Urinalysis of patients with kidney disease

No	Sample	Colour	Gross appearance	Specific grafity	pH	Protein	Erythrocytes	Leukcocytes	Urolith
1	Cat 1	Light yellow	Clear	1.010	6.5	30	Positive	Positive	Negative
2	Cat 2	Light yellow	Clear	1.017	6	15	Positive	Positive	Negative
3	Cat 3	Light red	Cloudy	1.020	**8**	2000	Positive	Negative	Struvite
4	Cat 4	Dark yellow	Cloudy	1.020	6.5	300	Positive	Positive	Negative
5	Cat 5	Light yellow	Clear	1.010	6.5	100	Negative	Positive	Negative
6	Cat 6	Light red	Clear	1.020	6.5	1000	Positive	Positive	Negative
7	Cat 7	Light yellow	Clear	1.015	5	0	Positive	Negative	Negative
8	Cat 8	Light red	Clear	1.020	7	1000	Positive	Negative	Struvite
9	Cat 9	Light yellow	Clear	1.020	6	100	Positive	Positive	Negative
10	Cat 10	Dark red	Cloudy	1.020	6.5	300	Positive	Negative	Struvite

Description: Normal urine is light yellow, clear, with a specific gravity of 1.010-1.020, a pH of 6-7, no erythrocytes, protein, and uroliths.

Renal ultrasonography revealed diverse abnormalities consistent with the clinical diagnoses. Observations included increased cortical echogenicity, irregular renal contours, and evidence of renal asymmetry or atrophy. Fig. 1 shows the representative sonograms.

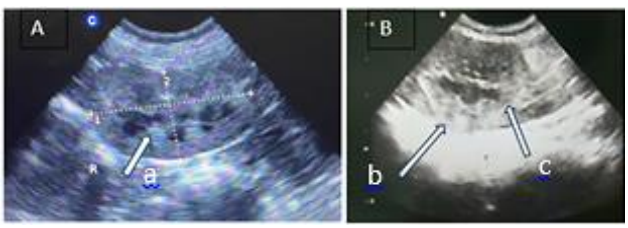

Fig. 1: Ultrasonography of feline patients with renal disease. (A) Cat 10 has hyperechoic, the boundary between the cortex and medulla is not clear (a). (B) Cat 1 has irregular renal contour (b), suggestive of polycystic kidney (c).

All cats received intramuscular administration of MSC-derived secretome at 0.2mL/kg body weight weekly for a maximum of eight weeks. However, only half of the cohort (five cats) were monitored through the full course due to mortality before treatment completion. Among the cats presenting with anemia, 50% demonstrated normalization of RBC levels by the end of therapy, while the remaining showed improvement though still below the standard range. The trend of RBC recovery during treatment is illustrated in Fig. 2.

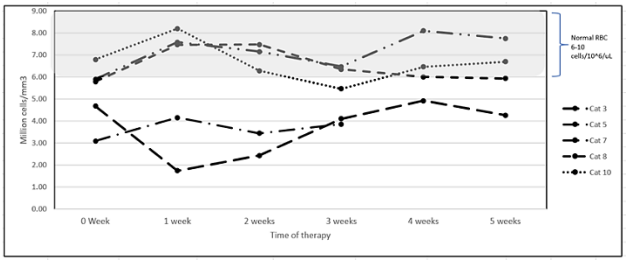

Fig. 2: Overview of RBC level development after 0.2mL/KgBW secretome therapy once a week.

In all monitored subjects, blood urea nitrogen (BUN) levels declined during the course of therapy. One male Persian cat exhibited a markedly elevated BUN concentration (>126mg/dL) prior to treatment. This cat received inpatient care including supportive fluid therapy and antibiotics. Following secretome administration, a

gradual decline in BUN was observed in all treated cats. However, some outpatient cases experienced transient increases in BUN, potentially due to suboptimal adherence to renal diets or inadequate hydration. By the end of the study, 80% of the treated cats had BUN levels within or approaching the normal reference range. The progression of BUN values over time is shown in Fig. 3.

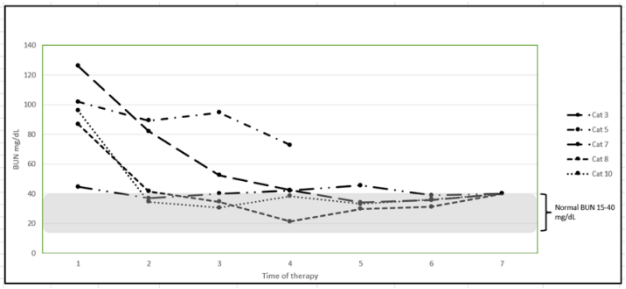

Fig. 3: BUN levels in cats with kidney disorders after undergoing secretome therapy of 0.2 mL/kg BW.

Creatinine, considered a more stable marker of renal filtration, was elevated in all cases at baseline. The highest level recorded (5.83mg/dL) was from a 1.5-year-old mixed-breed male with a prolonged history of urolithiasis. After receiving the complete course of secretome therapy, all surviving cats demonstrated reductions in serum creatinine. These outcomes are summarized in Fig. 4.

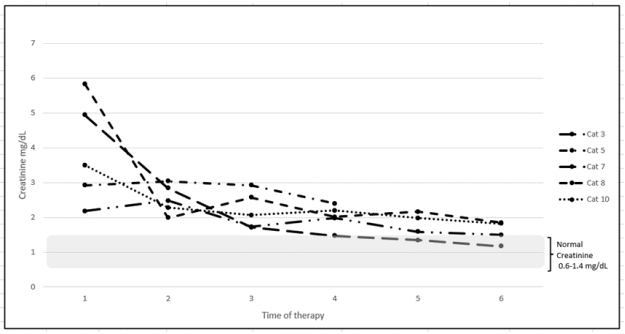

Fig. 4: Creatinine levels in cats with kidney disorders after undergoing secretome therapy of 0.2mL/kg BW.

Ultrasound reevaluation at the conclusion of therapy revealed improvements in renal morphology in 6 out of 10 cats. Specifically, those diagnosed with AKI exhibited decreased cortical thickening and enhanced corticomedullary definition, while cats with CKD showed stabilization of renal dimensions and marginal improvement in echogenic contrast. Comparative sonographic views pre- and post-treatment are presented in Fig. 5.

DISCUSSION

Distinguishing between acute kidney injury (AKI) and chronic kidney disease (CKD) in feline patients relies heavily on a combination of clinical observation, laboratory findings, and imaging modalities. Physical signs in AKI often include well-maintained body condition, painful or enlarged kidneys, and the absence of chronic symptoms such as prolonged weight loss or polyuria-polydipsia (Rimer et al. 2022). In contrast, CKD frequently presents with persistent clinical signs such as increased thirst and urination, anorexia, vomiting, and weight loss, which may be linked to the accumulation of uremic toxins that stimulate chemoreceptor zones in the brain (Larry and Francis 2016; Noviana et al. 2018; Martos and Villalba 2020).

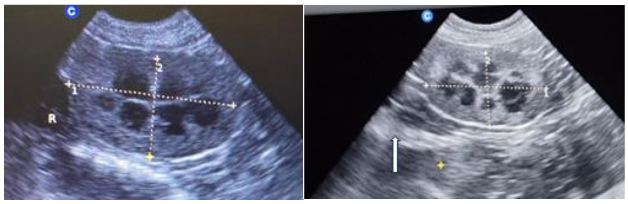

Fig. 5: Ultrasound image of cat kidney after 0.2ml/kg BB secretome therapy. Cat 10 has normal kidney size, there is a cortex and medulla with normal thickness

The dominant clinical findings in this study—anorexia, vomiting, lethargy, and weight loss—correspond with previous reports, which indicate these symptoms occur in more than 50% of cats with renal pathology (O'Neill et al. 2015). Anemia was identified in 80% of cases, possibly resulting from decreased erythropoietin production due to renal dysfunction, as well as reduced nutrient intake from anorexia. Studies suggest that 30–65% of cats with CKD experience anemia, primarily of the normocytic, normochromic, and non-regenerative type, with impaired erythropoietin synthesis being the key factor (Ettinger et al. 2016). In cases of AKI, increased packed cell volume (PCV) may reflect dehydration and hemoconcentration, although fluid loss is also common in CKD when fluid intake does not compensate for increased urinary output. The leukocytosis observed may indicate an acut inflammatory immune response, potentially associated with neutrophil activation during kidney injury (Villanueva et al. 2013; Wang et al. 2023).

Azotemia, marked by elevations in blood urea nitrogen (BUN) and creatinine, is a critical diagnostic feature in renal disease. Increased BUN levels can result from impaired glomerular filtration, excessive protein catabolism, gastrointestinal bleeding, or high-protein diets, while creatinine levels are more stable indicators of glomerular filtration (Larry and Francis, 2016). In this study, 60% of subjects fell within IRIS Stage 2 to 3, consistent with moderate azotemia (Jepson et al. 2009). Cats 3, 8, and 10 were diagnosed with AKI, most likely secondary to untreated urolithiasis, while cats 5 and 7 were classified as CKD based on their chronic clinical signs and imaging findings.

MSCs have been extensively studied in both precinical and clinical models for their regenerative capacity, primarily via paracrine activity. These cells release a wide array of soluble factors—cytokines, chemokines, growth factors, and extracellular vesicles—that contribute to anti-inflammatory, antifibrotic, and antiapoptotic processes, while also promoting tubular epithelial cell regeneration (Broekema et al. 2005). These molecules work in synergy to create a microenvironment conducive to renal tissue repair and immunomodulation (Tsuji et al. 2018; Cao et al. 2022).The secretome used in this study, derived from human umbilical cord MSCs using protocols established at

the Stem Cells and Cancer Institute. It contained key bioactive factors including hepatocyte growth factor (HGF), fibroblast growth factors (FGF-2 and FGF-7), stromal-derived factor-1, and vascular endothelial growth factor (VEGF), all of which have been implicated in epithelial cell proliferation, angiogenesis, and anti-inflammatory responses (Baglio et al. 2022; Mahmoud et al. 2024).

Various administration routes have been investigated for MSCs and their secretomes, including intraparenchymal, subcapsular and intravenous approaches, with multiple injections often yielding superior outcomes (IRIS 2009; Arifin et al. 2024). In this study, intramuscular delivery of the secretome over an eight-week period was associated with improvements in clinical condition, hematological indices, BUN and creatinine levels and renal architecture, especially among cats with AKI.

The therapeutic effects observed are consistent with previously reported mechanisms, including downregulation of proinflammatory mediators such as NF-κB and MMP9, suppression of C-reactive protein (CRP) and neutrophil gelatinase-associated lipocalin (NGAL), and attenuation of tissue inflammation, necrosis, and degeneration (Jepson et al. 2009; Tsuji et al. 2018). These molecular actions help mitigate tissue inflammation and support renal epithelial regeneration. Moreover, EVs and miRNAs within the secretome have been shown to influence macrophage polarization, thereby enhancing anti-inflammatory responses (Vizoso et al. 2017; Cao et al. 2022). Compared to conventional management strategies for feline renal disease, which often focus on symptomatic control (e.g., fluid therapy, dietary phosphorus restriction, antihypertensives), secretome therapy represents a regenerative approach aimed at restoring functional tissue integrity (Ranganath et al. 2012; Han et al. 2021). This cell-free strategy may overcome challenges associated with live cell transplantation, including immunogenicity, tumorigenicity, and storage instability.

Nevertheless, the findings of this study should be interpreted with caution due to limitations such as the small sample size, lack of a control group, and heterogeneity in disease stage. Future studies involving larger, randomized cohorts, standardized biomarker monitoring, and molecular profiling of renal recovery are necessary to confirm the clinical efficacy and safety of MSC-derived secretome in feline nephrology

Conclusion

This pilot study provides preliminary but compelling evidence that secretome therapy derived from human umbilical cord mesenchymal stem cells (hUC-MSCs) offers therapeutic benefits for cats suffering from acute and chronic kidney disease. Administered intramuscularly at a dose of 0.2 mL/kg once weekly for up to eight weeks, the secretome was associated with clinical improvements in appetite, hydration, and energy levels, alongside measurable reductions in blood urea nitrogen (BUN) and serum creatinine concentrations. Ultrasonographic assessments revealed favorable morphological changes in renal structure, particularly in acute kidney injury (AKI) cases. These findings highlight the secretome's potential to serve as a regenerative, cell-free intervention that circumvents the immunologic and logistical challenges associated with direct stem cell transplantation. Future research with larger, randomized controlled trials and mechanistic analyses will be essential to validate these findings and establish the safety, efficacy, and molecular basis of MSC-derived secretome therapy in feline nephrology.

DECLARATIONS

Funding: This research was funded by Universitas Gadjah Mada, Yogyakarta, Indonesia through Academic Excellent Research Program 2024 number 431/UN1.P1/KPT/HUKOR/2024.

Acknowledgement: Tnaks are expressed to the Chancellor of Universitas Gadjah Mada, Yogyakarta, Indonesia, Dean Faculty of Veterinary Medicine Universitas Gadjah Mada fot their permission to carry out this research. Appreciation is also extended to the leadership and staff of Prof. Soeparwi Animal Hospital and Internal Medicine Clinic in Faculty of Veterinary Medicine Universitas Gadjah Mada, Yogyakarta, Indonesia for all their assistance in carrying out the research. Thank you also to the clients, for allowing their beloved cats to be treated with secretome therapy.

Conflict of Interest: The authors declare that no commercial or financial relationships could be construed as a potential conflict of interest in conducting the research. The owners have approved the use of cats as research subjects by signing an informed consent.

Data Availability: ???

Ethics Statement: Patients from Professor Soeparwi Animals Hospital, Faculty of Veterinary Medicine, Universitas Gadjah Mada were used in this research. Each cat used in this study had obtained permission from the owner through informed consent.

Author's Contribution: GTM: collected samples, secretome therapy, laboratory analysis. YHF conducted research in the laboratory, delivered reagents/materials, and secretome production. TBP wrote the manuscript examined the data, and wrote and critically revised the manuscript. All authors read and approved the final manuscript.

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REFERENCES

Arifin, Purwanto B, Indarto D, Wasita B, Sumanjar T,

Pamungkasari EP and Soetrisno, 2024. Improvement of renal functions in mice with septic acute kidney injury using secretome of mesenchymal stem cells. Saudi Journal of Biological Sciences 31:103931. https://doi.org/10.1016/j.sjbs.2024.103931

Baglio SR, Pegtel DM and Baldini N, 2022. Mesenchymal stem cell-secreted extracellular vesicles: a novel therapeutic approach for tissue regeneration. Current Opinion in Pharmacology 64:102204. https://doi.org/10.3389/fphys.2012.00359

Bartges JW, 2012. Chronic kidney disease in dogs and cats. Veterinary Clinic North America Small Animals Practice 42: 669-692. https://doi.org/10.1016/j.cvsm.2012.04.008

Bezerra GSJ, Srisawat N, Galdino GS, Macedo ES , Pinto JR, Farias GMN, Alencar RL, Neto RJP, Barros EJG and Daher EDF, 2018. Acute kidney injury in leptospirosis: overview and perspectives. Asian Pacific Journal Tropical Medicine 11:5. http://dx.doi.org/10.4103/1995-7645.244514

Broekema M, Martine HC, Koerts JA, Petersen AH, Van Luyn MJA, Navis G and Popa RR, 2005. "Determinants of tubular bone marrow-derived cell engraftment after renal ischemia/reperfusion in rats," Kidney International 68(6):2572–2581. https://www.kidney-international.org/issue/S0085-2538(05)X8600-8

Cao Q, Huang C, Chen XM and Pollock CA, 2022. Mesenchymal stem cell-derived exosomes: toward cell-free therapeutic strategies in chronic kidney disease. Frontiers in Medicine 9:816656. https://doi.org/10.3389/fmed.2022.816656

Chen L, Tredget EE, Wu PYG and Wu Y, 2008. Paracrine Factors of Mesenchymal Stem Cells Recruit Macrophages and Endothelial Lineage Cells and Enhance Wound Healing. PLoS One 3:e1886. 2008. https://doi.org/10.1371/journal.pone.0001886

Ettinger SJ, Edward C, Feldman and Cote E, 2016. Textbook of Veterinary Internal Medicine Expert Consult. 8th Edition, Saunder.

Griffith JD and Johnson SA, 2022. Textbook Of Veterinary Physiology. Elsevier.

Han Q, Wang X, Ding X, He J, Cai G and Zhu H, 2021. Immunomodulatory effects of mesenchymal stem cells on drug-induced acute kidney injury. Frontiers in Immunology 12:683003. https://doi.org/10.3389/fimmu.2021.683003

Harel Z, Bell CM, Dixon SN, McArthur E, James MT, Garg AX, Harel S, Silver S and Wald R, 2014. Predictors of progression to chronic dialysis in survivors of severe acute kidney injury: Acompeting risk study. BMC Nephrology 15: 114. https://doi.org/10.1186/1471-2369-15-114

Harvey JW and Bruss ML, 2021. The Kidney. In Textbook Of Veterinary Internal Medicine.Elsevier.

Hasegawa S, Jao TM and Inagi R, 2017. Dietary Metabolites and Chronic Kidney Disease. Nutrients 9: 358. https://doi.org/10.3390/nu9040358

Ilic D and Ogilvie C, 2017. Concise review: human embryonic stem cells-what have we done? What are we doing? where are we going? 2017. Stem Cells 35:17–25. https://doi.org/10.1002/stem.2450

International Renal Interest Society. Staging of CKD. 2009. https://www.iris-kidney.com/iris-guidelines-1

Jepson RE, Brodbelt D, Vallance C, Syme HM and Elliott J, 2009. Evaluation of predictors of the development of azotemia in cats. Journal of Veterinary Internal Medicine 23: 806–13. https://doi.org/10.1111/j.1939-1676.2009.0339.x

Larry PT and Francis WKS, 2016. Blackwell's five-minute veterinary consult: Canine and feline. John Wiley & Sons Inc, Iowa USA, 6th ed. p. 1416.

Lee JS, Hong JM, Moon GJ, Lee PH, Ahn YH and Bang OY, 2010. A Long-Term Follow-Up Study of Intravenous Autologous Mesenchymal Stem Cell Transplantation in Patients With Ischemic Stroke. Stem Cells Journal 28(6):1010-1106. https://doi.org/10.1002/stem.214

Lund EM, Armstrong PJ, Kirk CA, Kolar LM and Klausner JS, 1999. Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. Journal of American Veterinary Medicine Association 214(9):1336-41. http://dx.doi.org/10.2460/javma.1999.214.09.1336 .

Mahmoud AM, Mousa SA and Elhamamsy HT, 2024. Evaluation of serum cystatin c and associated clinical and biochemical changes in acute and chronic renal dysfunction in dogs. Egyptian Journal of Veterinary Sciences 1–13. https://doi.org/10.21608/ ejvs.2024.315104.2335

Martos CMP and Villalba IL, 2020. *Servet Clinical Guide Chronic Kidney Disease*. Servet.

McLeland SM, Lunn KF, Duncan CG and Quimby JM, 2014. Relationship among serum creatinine, serum gastrin, calcium-phosphorus product, and uremic gastropathy in cats with chronic kidney disease. Journal of Veterinary Internal Medicine 28(3):827-37. https://doi.org/ 10.1111/jvim.12342

Morigi M, Imberti B, Zoja C, Corna D, Tomasoni S, Abbate M, Rottoli D, Angioletti S, Benigni A, Perico N and Alison M, 2004. Mesenchymal stem cells are renotropic, helping to repairthe kidney and improve function in acute renal failure. Journal of the American Society of Nephrology 15(7):1794–804. https://doi.org/10.1097/01.asn.0000128974.07460.34

Noviana D, Aliambar SH, Ulum MF and Siswandi R, 2018. Diagnosis Ultrasonografi pada Hewan Kecil. IPB Press, Bogor, Indonesia

O'Neill DG, Church DB, McGreevy PD, Thomsonm PC and Brodbelt DC, 2015. Longevity and mortality of cats attending primary care veterinary practices in England. Journal of Feline Medicine Surgery 17:125-133. https://doi.org/10.1177/1098612X14536176

Polzin DJ, 2010. Chronic kidney disease, 2010. In: Ettinger, SJ, Feldman EC. Textbook of Veterinary Internal Medicine. Philadelphia, PA: Saunders WB 1955-2115.

Prihatno SA, Padeta I, Larasati AD, Sundari B, Hidayati A, Fibrianto YH and Budipitojo T, 2018. Effects of secretome on cisplatin-induced testicular dysfunction in rats. Veterinary World 11(24):1349-1356. https://www.veterinaryworld.org/Vol.11/No.9.php

Ranganath SH, Levy O, Inamdar MS and Karp JM, 2012. Harnessing the mesenchymal stem cell secretome for the treatment of cardiovascular disease. Cell Stem Cell 10, 244–258. http://dx.doi.org/10.1016/j.stem.2012.02.005

Rimer D, Chen H, Bar-Nathan M and Segev G, 2022. Acute kidney injury in dogs: Etiology, clinical and clinicopathologic findings, prognostic markers, and outcome. Journal of Veterinary Internal Medicine 36:609–618. https://doi.org/10.1111/jvim.16375

Ross L, 2014. Acute kidney injury in dogs and cats. Veterinary Clinics of North America: Journzl of Small Animals Practive 1(1): 1-14. https://doi.org/10.1016/j.cvsm.2010.09.003

Segev G, Cortellini S, Foster JD, Francey T, Langston C, Londoño L, Schweighauser A and Jepson RE, 2024. International renal interest society best practice consensus guidelines for intermittent hemodialysis in dogs and cats. The Veterinary Journal 305: 106092. https://doi.org/10.1016/j.tvjl.2024.106068

Semedo P, Correa-Costa M, Cenedeze AM, Malheiros MACD, dos Reis AM, Shimizu MH, Seguro AC, Pacheco-Silva A and Camara SNO, 2009. Mesenchymal stem cells attenuate renal fibrosis through immune modulation and remodeling properties in a rat remnant kidney model. Stem Cells 27: 3063–3073. https://doi.org/10.1002/stem.214

Seung-Jun L, Min-Ok R, Min-Soo S, Sang-Bum P, Jin-Ok A, Sei-Myoung H, Kyung-Sun K, Dong-Ha B and Hwa-Young Y, 2017. Mesenchymal Stem Cells Contribute to Improvement of Renal Function in a Canine Kidney Injury Model. In Vivo 31(6):1115-1124. https://doi.org/10.21873/invivo.11177

Tsuji K, Kitamura S and Wada J, 2018. Secretomes from

Mesenchymal Stem Cells against Acute Kidney Injury: Possible Heterogeneity. Stem Cells International Article ID 8693137, 14 pages. https://doi.org/10.1155/2018/8693137

Villanueva S, Carreño J E, Salazar L, Vergara C, Strodthoff R, Fajre F, Cespedes C, Saez PJ, Irarrazabal C, Bartolucci J, Figueroa F and Vio CP, 2013. Human mesenchymal stem cells derived from adipose tissue reduce functional and tissue damage in a rat model of chronic renal failure. Clinical. Science. (London) 125(4):199-210. https://doi.org/10.1042/CS20120644

Wang S, Cai Q, Zhao W, Liu Y, Zhang Y and Wang L, 2023. Neutrophil extracellular traps promote AKI in sepsis by activating the STING pathway in tubular epithelial cells. Cell Death & Disease 14(6):416. https://doi.org/10.1038/s41420-023-01614-8