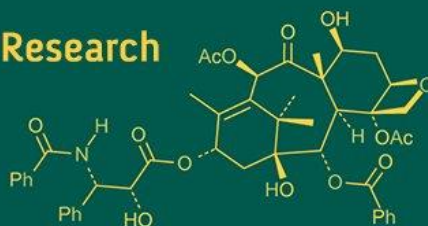


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Haemato-biochemical and urinary alterations in dogs undergoing iohexol plasma clearance for glomerular filtration rate assessment

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Abstract

Iohexol plasma clearance is widely applied for estimating glomerular filtration rate (GFR) in dogs, yet there is limited documentation regarding its immediate effects on routine laboratory parameters. The present study was conducted to evaluate haematological, serum biochemical, and urinary changes in apparently healthy dogs undergoing iohexol-based GFR assessment. Dogs presented for routine health evaluation and vaccination were screened before inclusion. Each animal underwent detailed clinical examination along with hematobiochemical testing, urinalysis, blood pressure measurement, and renal ultrasonography with Doppler assessment. Only dogs considered clinically normal according to IRIS guidelines, thereby excluding acute kidney injury (AKI) and chronic kidney disease (CKD), were enrolled. Six dogs that met the selection criteria were included with owner consent. Iohexol was administered intravenously as a single bolus at a dose of 300 mg iodine/kg body weight for plasma clearance estimation of GFR. Blood and urine samples were collected before and after administration to assess possible changes. Statistical comparison of pre- and post-procedure values showed no significant differences in erythrocyte indices, leukocyte counts, platelet numbers, renal biomarkers, serum electrolytes, or urinary parameters. All recorded values remained within accepted physiological limits. Overall, iohexol was well tolerated, and no adverse clinical or haemato-biochemical and urinary alterations were observed. These findings support the safety of iohexol plasma clearance as a practical method for GFR estimation in healthy dogs.

Keywords: Iohexol, dog, hematobiochemical, urinalysis, glomerular filtration rate

Introduction

The kidneys play a central role in maintaining internal stability by regulating fluid balance, electrolytes, and the excretion of metabolic waste. They remove excesses to restore balance and preserve vital compounds during deficits. To avoid toxicity, nitrogenous wastes such as urea and creatinine are excreted, while nutrients such as glucose and amino acids are properly absorbed. The kidneys not only produce hormones such as renin, erythropoietin, and prostaglandins, but they also activate vitamin D and help maintain acid-base balance. Their primary function is to filter blood at the glomerulus and then regulate the filtrate via the renal tubules to maintain the extracellular fluid composition required by the body (Finco, 1997)^[1].

Glomerular filtration rate (GFR) is defined as the volume of plasma filtered by the glomeruli per unit time, serving as a key indicator of overall kidney function. It reflects how effectively the kidneys are clearing waste and maintaining fluid and electrolyte balance. Compared to traditional markers such as serum creatinine, GFR is more sensitive in detecting early declines in renal performance. Glomerular filtration rate (GFR) is regarded as the most sensitive indicator of kidney disease, as it is directly linked to the number of working nephrons. Despite its clinical value, the use of GFR measurement remains limited in veterinary practice. GFR measurement can reveal hidden renal impairment when serum creatinine levels are at the higher end of the normal range or only slightly elevated. Determining whether decreased urine concentration is the result of early kidney insufficiency is especially useful in polyuric, non-azotemic dogs. Furthermore, by serving as a screening tool for breeds that are prone to hereditary nephropathies, GFR testing aids in monitoring and selective breeding.

A precise GFR evaluation facilitates the early detection of nephrotoxicity and supports modified drug dosage in animals with compromised renal function (Willson and Pressler, 2011) [2].

Clearance is a measure of an organ's capacity to remove a material from the body; it is the volume of plasma from which the substance is entirely eliminated per unit of time. In particular, renal clearance refers to the volume of plasma that the kidneys remove from a substance per unit of time, which indicates kidney function and the quantity of material expelled in urine. Plasma clearance measures the volume of plasma from which a substance is completely removed per unit time, providing an estimate of glomerular filtration rate (GFR) when the marker is filtered solely by the glomerulus (Hall and Hall, 2021) [3].

Several markers are used in dogs and cats to assess GFR. Inulin is considered the gold standard due to its precision; however, its routine use is limited due to the complexity in measuring it. Creatinine, both endogenous and exogenous, is widely applied, though values may be influenced by body weight and analytical methods. Radiolabelled tracers such as Tc-DTPA and Cr-EDTA give reliable results but require specialized equipment. Of all these, Iohexol has gained preference for plasma clearance studies because of its safety and reproducibility, though differences in analytical methods can affect results (Wilson and Pressler, 2011) [2].

Iohexol, chemically described as N, N-bis(2,3-dihydroxypropyl)-5- [N-(2,3-dihydroxypropyl)-acetamido]-2,4,6-triiodo-isophthalamide, is a non-ionic, water-soluble monomeric contrast agent with a molecular weight of 821.14 (Krutzen, 1984) [4]. It is widely regarded as an ideal marker for assessing glomerular filtration rate (GFR) because it is cleared exclusively by glomerular filtration and does not undergo tubular secretion or reabsorption, ensuring accurate measurement of renal function.

Urine analysis is a common part of clinical examination for dogs and provides important information about the health of the animal. Color, pH, urine specific gravity (USG), protein levels, and the presence of compounds including glucose, bilirubin, and ketones are often measured factors. In addition to providing crucial diagnostic information about renal illnesses, metabolic problems including diabetes, urinary infections, and urolith development, it is a useful screening technique for animals that do not exhibit symptoms (Decramer *et al.*, 2008) [5]. When protein is present in urine, it is known as proteinuria. Normally, the glomerular filtration barrier prevents this from happening, and the renal tubules restore it. When urinary tract illness is absent, persistent proteinuria often signifies renal injury. The test of choice for animal proteinuria is currently the urine protein-to-creatinine ratio (UP/C), which closely correlates with the 24-hour measurement and offers a dependable estimate of daily protein excretion from a single random urine sample (Harley and Langston, 2012) [6]. Urine protein-to-creatinine ratio (UPC) assays and semiquantitative dipsticks can be used to evaluate proteinuria. Proteinuria is indicated by urinary protein-to-creatinine ratios higher than 300 mg/day (DiBartola, 2006) [7]. UPC, or 24-hour urine protein excretion, is a valuable tool for assessing the severity of chronic proteinuria.

A basic diagnostic tool for detecting urine abnormalities and evaluating kidney health is urinalysis. It is one of the best non-invasive and cheaper technique for identifying early renal dysfunction or failure. Protein, glucose, ketone bodies,

and other substances leak out of the kidneys into the urine when the kidneys become dysfunctional because of structural or functional damage (Athaley *et al.*, 2018) [8]. Renal damage may be indicated by urinalysis results such as glycosuria and proteinuria (Piech and Wycislo, 2018) [9]. Following the exclusion of prerenal and postrenal sources, the urine protein to creatinine ratio can be used to measure urinary protein loss (Lees *et al.*, 2005) [10].

Renal disease, glomerular dysfunction, high blood pressure, immune-related glomerulopathies, inflammatory kidney conditions, and pyelonephritis can all lead to an increase in the UPC ratio. However, urinary tract infection might result in false positive results. The UPC ratio produces false findings due to proteinuria caused by UTI, Post study-renal inflammation and diseases, and urinary stones (Schmid, 2022) [11].

Materials and Methods

Selection Criteria

Of 1,180 newly registered cases of dogs, 210 dogs were brought in for routine health checkup and vaccination. Most dogs showed no unusual signs on clinical examination and blood smear examination showed no evidence of any haemoprotozoan infections. From this group, six apparently healthy dogs were selected after obtaining the owner's consent.

Sample Collection and Procedures

The whole blood samples (5 ml) were obtained from the cephalic or saphenous vein both prior to (0 hr) and following Iohexol (8-10 hrs) administration. Blood samples collected in vacutainers with K3EDTA were used for haematological analysis on the same day, whereas serum and plasma were separated and used immediately or stored at -20 °C till further use.

Various haematological parameters (Hb., PCV, TLC, TEC, Platelets, MCV, MCH, MCHC) were estimated using automatic blood cell counter (MEK-6420P, Nihon Kohden, India). Renal biomarkers like Creatinine (mg/dl) and Blood Urea Nitrogen (mg/dl) were estimated using serum samples. The renal health status of all the dogs under study was evaluated as per IRIS guidelines of Acute Kidney Injury (AKI) (2016) and Chronic Kidney Dysfunction (CKD) (IRIS, 2023).

Approximately 5-10 ml of urine samples were aseptically collected from each dog via catheterization both prior to (0 hr) and following Iohexol (8-10 hrs) administration. Thereafter, various physical (colour, transparency, pH and specific gravity) and chemical parameters (Protein, blood, ketone bodies, glucose, nitrite, leukocytes *etc.*) were estimated using commercially available urine analysis strips in the semi-automated urine analyser. Urine Protein to Creatinine ratio (UPC) was also estimated from the collected urine samples.

Pre- and post-administration data were compared statistically using Student's t-test ($p \leq 0.05$).

Results and Discussion

Assessment of Clinical and Physiological Parameters of Dogs under Study

All dogs ($n = 6$) showed normal appetite, urine output, defecation, demeanour, and conjunctival mucous membrane colour after Iohexol clearance study period. During the study period and after Iohexol clearance study period, no

one showed signs of vomiting, diarrhoea, haematuria, or melena. Physiological parameters such as capillary refill time (CRT), heart rate, respiratory rate, and rectal temperature were recorded both before and after the administration of iohexol, and they were all within the normal reference range recommended for dogs (Feldman and Ettinger, 2017) ^[12] (Table-1). Similar to our findings, Dewangan *et al.* (2025) ^[13] found no appreciable changes in physiological parameters after administering iohexol.

Table 1: Clinico-physiological examinations of dogs under study (n = 6)

S. N.	Parameters	Mean $\pm$ SE		p value
		Pre study	Post study	
1	Temperature ($^{\circ}$ F)	100.88 $\pm$ 0.50	101.16 $\pm$ 0.44	0.69
2	Heart rate (beats/min)	80.66 $\pm$ 3.33	86.33 $\pm$ 3.38	0.28
3	Respiration Rate (breaths/min)	24.33 $\pm$ 1.05	26.33 $\pm$ 0.96	0.20
4	Capillary refill time (sec)	0.91 $\pm$ 0.15	0.91 $\pm$ 0.14	1.00

Assessment of Haemato-Biochemical Parameters of Dogs Under Study

Various haematological parameters including haemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), platelet count and erythrocyte indices were remained within normal physiological limits before and after Iohexol clearance study period and there were non-significant differences in values of these parameters before and after the study (Brar *et al.*, 2002 ^[14]; Kim *et al.*, 2020) ^[15] (Table-2). Our findings are in accordance with the reports of Kaenkongploo *et al.* (2022) ^[16] and Dewangan *et al.* (2025) ^[13], who had reported non-significant differences in haematological parameters following iohexol clearance studies. The stability of erythrocyte indices further supported that iohexol administration did not induce haematological stress or renal-associated alterations, as reductions in Hb and PCV are generally seen in renal dysfunction as reported by Polzin (2011) ^[17] and Grauer (2005) ^[18]. During study, the mean $\pm$ SE values of MCV, MCH, and MCHC in dogs also remained within the established reference range. Similarly, Lippi *et al.* (2021) ^[19] found non-significant difference in such values during and after Iohexol clearance study.

In all dogs, values of BUN, creatinine and electrolytes remained within the normal reference range and showed non-significant difference between the groups. The results suggesting that Iohexol at the dosage employed in this investigation had no negative effects on renal biochemical parameters (Table-3). Similar observations were made by Kirberger *et al.* (2012) ^[20], who reported no significant alteration in serum creatinine following Iohexol administration. Cagnasso *et al.* (2021) ^[21] also reported that most of the routine serum biochemical analytes showed non-significant difference in their values on administration of Iohexol. Izci *et al.* (2004) ^[22] also reported that serum electrolyte concentrations remained stable post iohexol administration. In a report from India, Sharma *et al.* (2015) ^[23] also found non-significant differences in electrolytes and creatinine during study period which is indicating that Iohexol does not interfere with electrolyte balance. On contrary, Dewangan *et al.* (2025) ^[13] observed a transient increase in serum urea nitrogen and creatinine at one hour after administration of a much higher dose of iohexol, with values returning towards baseline within 24 hours.

Table 2: Haematological analysis of dogs under study (n = 6)

S. N.	Parameters	Mean $\pm$ SE		p value
		Pre study	Post study	
1	HB (gm%)	12.48 $\pm$ 0.42	12.35 $\pm$ 0.36	0.21
2	PCV (%)	42.11 $\pm$ 1.58	41.16 $\pm$ 0.43	0.56
3	TEC ($\times 10^6$ /cmm)	5.91 $\pm$ 0.15	5.81 $\pm$ 0.10	0.39
4	Platelets ($\times 10^3$ /cmm)	2.84 $\pm$ 0.11	2.85 $\pm$ 0.08	0.93
5	TLC ($\times 10^3$ /cmm)	10.591 $\pm$ 0.791	9.386 $\pm$ 0.291	0.16
6	Neutrophils (%)	74.66 $\pm$ 3.06	73.83 $\pm$ 2.91	0.29
7	Lymphocytes (%)	18.6 $\pm$ 2.84	18.83 $\pm$ 2.63	0.70
8	Eosinophils (%)	3.50 $\pm$ 0.42	3.50 $\pm$ 0.39	1.00
9	Basophils (%)	2.83 $\pm$ 0.30	3.16 $\pm$ 0.28	0.53
10	MCV (fl)	67.5 $\pm$ 0.76	67.66 $\pm$ 0.87	0.89
11	MCH (pg)	21.5 $\pm$ 0.76	21 $\pm$ 0.52	0.61
12	MCHC (g/dL)	33.83 $\pm$ 1.16	33.5 $\pm$ 0.69	0.81

Table 3: Various biochemical parameters of dogs under study (n = 6)

S. N.	Parameters	Mean $\pm$ SE		p value
		Pre study	Post study	
1	BUN (mg/dl)	24.31 $\pm$ 1.29	22.66 $\pm$ 1.11	0.25
2	Creatinine (mg/dl)	1.32 $\pm$ 0.07	1.29 $\pm$ 0.05	0.21
3	Sodium (Na ⁺) (mEq/l)	144.06 $\pm$ 2.23	143.86 $\pm$ 1.91	0.94
4	Potassium (K ⁺) (mEq/l)	4.37 $\pm$ 0.19	4.35 $\pm$ 0.18	0.90
5	Chloride (Cl ⁻) (mEq/l)	110.11 $\pm$ 3.08	107.14 $\pm$ 1.88	0.11
6	Phosphorus (P) (mg/dl)	3.31 $\pm$ 0.28	3.50 $\pm$ 0.18	0.41

Quantitative and Qualitative Urine Analysis of Dogs Under Study

During study, no changes in colour, consistency and turbidity in urine samples were observed. These results are comparable to findings of Kirberger *et al.* (2012) ^[20] who noted no changes in urine colour, consistency and turbidity post Iohexol study. Similarly, Dewangan *et al.* (2025) ^[13] and Sharma *et al.* (2015) ^[23] also observed no changes in urine parameters after administering Iohexol at higher doses such as 1100 mg I/kg and 600 mg I/kg, respectively. This confirms that Iohexol, whether used at low doses for GFR estimation or at higher doses for contrast studies, does not exert measurable effects on routine urinalysis in dogs.

Quantitative urine evaluation showed (Table-4) that urine pH and specific gravity remained within normal physiological limits before and after Iohexol administration. The urine protein-to-creatinine ratio was also within the reference range for healthy dogs, confirming the absence of proteinuria. Our findings are in accordance with findings of McGlynn *et al.* (2023) ^[24] who also reported non-significant differences in UPC during Iohexol clearance study.

Table 4: Quantitative urine analysis in dogs under study

S. N.	Parameters	Mean $\pm$ SE		p value
		Pre study	Post study	
1	Urine pH	7.16 $\pm$ 0.60	6.83 $\pm$ 0.51	0.36
2	Urine Specific gravity	1.020 $\pm$ 0.002	1.019 $\pm$ 0.002	0.17
3	Urine Protein to Creatinine ratio (UPC)	0.20 $\pm$ 0.07	0.18 $\pm$ 0.05	0.18

Conclusion

Intravenous administration of Iohexol at a dose of 300 mg iodine/kg body weight for estimation of glomerular filtration rate did not result in any significant alterations in haematological, serum biochemical, or urinary parameters in apparently healthy dogs under study. All measured variables remained within accepted physiological reference limits following the procedure. No adverse clinical findings were

observed during and after the study period. These results indicate that GFR estimation using Iohexol plasma clearance test does not adversely influence systemic or renal parameters in apparently healthy dogs.

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