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Effect of Unilateral Ureteral Ligation on Blood Constituents, Renal Histopathology and Ultrasonography in Dogs

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Abstract: The goal of the present study was to evaluate the effect of unilateral ureteral ligation on blood constituents, renal histopathology and ultrasonography in dogs. A total number of 25 apparently healthy adult mongrel dogs belong to Assiut city, Egypt were subjected to study. Animals were divided into 5 equal groups; the left ureter was ligated for 2, 7, 14 and 21 days in group I, II, III and IV, respectively. Group V represented the control group. The animals of the groups I-IV were euthanized on days 2, 7, 14 and 21, respectively. Right and left uretronephrectomies were performed and specimens were taken for the histopathological examination. Results revealed significant increases in total leucocytes and neutrophils counts from day 2-17. There were significant decreases ($p<0.01$) in total RBCs count and PCV% at day 14. Creatinine level was significantly increased on days 7 and 17. Histopathological changes were varied from glomerular swelling and congestion to glomerular atrophy.

Key words: Dog, haematology, histopathology, serum, ureter, ligation

INTRODUCTION

Acute obstructive uropathy is a worldwide major cause of renal impairment that leads to end-stage renal failure if left untreated (Harris *et al*., 1993). Urinary obstruction, together with infectious processes continuous to be the most frequent consequences of diseases that affect the urinary tract, potentially causing renal parenchymal damage of an irreversible nature (Tucci *et al*., 1997).

Hydronephrosis has traditionally been used to describe pelvic distension of the kidney secondary to obstruction, infection or trauma (Cartee *et al*., 1980; Ackerman, 1983). It refers to dilation of the renal pelvis and calyces resulting in progressive atrophy and cystic enlargement of renal parenchyma (Felkai *et al*., 1995; Finco 1995; Jones *et al*., 1997; Nyland *et al*., 2002). The changes in renal morphology in response to complete unilateral ureteral obstruction depend on time of onset, duration and degree of obstruction. Hydronephrotic atrophy may be associated with destruction of all the renal parenchymal tissue and a thin-walled sac of watery fluid remains. The time course for this is unknown in humans but in rats it takes about 4 months in rabbits 10 months and in dogs 18 months or more after onset of obstruction (Fink *et al*., 1980). However, the acutely obstructed kidney may increase its weight within hours after onset of obstruction due to renal parenchymal edema (Moody *et al*., 1977). Creatinine is the analyte most frequently measured in human and veterinary clinical chemistry laboratories as an indirect measure of Glomerular Filtration Rate (GFR). Plasma creatinine (P-creatinine) originates from the degradation of creatine and creatine phosphate which are present mainly in muscle and in food.

Creatinine is cleared by glomerular filtration with negligible renal secretion and extrarenal metabolism and its clearance is a good estimate of GFR. Pre-analytical factors such as age and breed can have an impact on P-creatinine concentration while many intraindividual factors of variation have little effect. Dehydration and drugs mainly affect P-creatinine concentration in dogs by decreasing GFR. P-creatinine is increased in renal failure whatever its cause and correlates with a decrease in GFR (Braun *et al*., 2003). The present study was undertaken to evaluate the effect of unilateral ureteral ligation on blood constituents, renal histopathology and ultrasonography in dogs.

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MATERIALS AND METHODS

Animals: A total number of 25 apparently healthy adult mongrel dogs belong to Assiut city, Egypt were subjected to study, their ages ranged from 9 months to 4 years and their weight from 9-31 kg body weight Animal experiments were conducted according to the guidelines for animal experiments in Assiut University, Egypt.

Animals were divided into 5 equal groups; the left ureter was ligated for 2, 7, 14 and 21 days in group I-IV, respectively. Group V represented the control group. The control group was subjected to ventral abdominal celiotomy and visceral manipulation without ureteral ligation and represents the control group.

Animals were anaesthetized by intravenous injection of thiopental sodium after diazepam tranquilization. Surgery was performed under complete aseptic conditions. All animals were subjected to ventral abdominal celiotomy. Unilateral left sided ureteral ligation was performed near the uretrovesicular junction in the animals of groups I-IV. Antibiotic spray (Alamycin spray (Norbrook Laboratories Limited. Newry. BT35 6JP. N. Ireland)) was applied on the skin of the operative field after skin closure.

Euthanasia was done by the rapid intravenous injection of a lethal dose of sodium thiopental. The animals of the groups I-IV were euthanized on days 2, 7, 14 and 21, respectively. Right and left uretronephrectomies were performed and specimens were taken for the histopathological examination.

Ultrasonogaraphic examinations: The ultrasonographic examination of both kidneys was carried out preoperatively and on days 2, 7, 14 and 21 postoperatively according to Burk and Feeney (2003). A 5 MHz sector transducer was used for renal ultrasonography. The kidneys were examined by ventral approach with the animal in dorsal recumbency. The lateral approach was used for the ultrasonographic examination in case of obese animals specially females with rounded contour abdomen. The examination planes were transverse and sagittal section.

Samples: Blood samples were collected from the recurrent tarsal vein for haematological and serum biochemical analysis on days 0 and 2 for group I, on days 0, 3 and 7 for group II, on days 0, 10 and 14 for group III and on days 0, 17 and 21 for group IV. For the control group, blood samples were collected on days 0, 2, 3, 7, 10, 14, 17 and 21.

Haematological analysis: Whole blood samples were collected in vacutainer tubes containing EDTA (Ethylene Daiamine Tetraacetic Acid) as anticoagulant and were subjected to haematological analysis according to Coles (1986). Total Red Blood Cells (TRBCs) count and Total White Blood Cells (TWBCs) count were measured using haemocytometer method. Haemoglobin concentration was measured by using commercial test kits supplied by spectrum diagnostics (Spectrum Diagnostics, Cairo, Egypt) and by Digital VIS/Ultraviolet Spectrophotometer (Cecil instruments, Cambridge, England, series No. 52.232). Packed Cell Volume (PCV%) was measured using microhaematocrit method. Mean Corpuscular Value (MCV, fl), Mean Corpuscular Haemoglobin (MCH, pg) and Mean Corpuscular Haemoglobin Concentration (MCHC, g dL^{-1}) were calculated mathematically. A drop of blood was spread on blood film, air dried, fixed in absolute methyl alcohol and stained by Giemsa stain was used for differential leucocytic count.

Biochemical analysis: Blood samples for separation of serum were collected in plain vacutainer tubes and processed for separation of serum according to Coles (1986). Serum samples were used for measuring serum total protein, albumin, Blood Urea Nitrogen (BUN), creatinine using commercial test kits supplied by spectrum diagnostics (Egyptian company for biotechnology, Cairo, Egypt) and by means of digital VIS/Ultraviolet spectrophotometer (Cecil instruments, Cambridge, England, series No. 52.232). Serum creatinine clearance was calculated by the Cockroft-Gault equation as follows: Creatinine clearance = (140 - age [year] x (patient's weight [kg])/72x (serum creatinine [mg dL^{-1}]) (Gonenci *et al*., 2003).

Histopathological examination: For histological examination, tissue specimens were obtained from kidneys after euthanasia. Specimens were fixed in 10% neutral buffered formalin, dehydrated in a graded alcohol series, cleared with methyl benzoate and embedded in paraffin wax. Sections of 5 μm were cut and stained with haematoxylin/eosin for light microscopic examination (Bancroft *et al*., 1996).

Statistical analysis: Statistical analysis was conducted using SPSS 16.0 for windows (SPSS, Chicago, USA). Data for group I was compared using one way ANOVA. Data from other groups were tested for difference using Post-hoc test, Least Significant Difference (LSD). Statistically significant differences were determined at $p = 0.05$. Data were expressed as Mean±SD.

RESULTS AND DISCUSSION

Ultrasonographic findings

Group I: Ultrasonography of the left kidney showed that the renal corex and medulla was easily demarcated. The coticomedullary junction was obvious. The echogenicity of the renal parenchyma (cortex and medulla) showed no changes (Fig. 1). There was no clear difference between the right kidney pre and post-operatively. The echogenicity of the renal parenchyma had no changes.

Group II: Ultrasonography of the left kidney showed clearly demarcated cortex. The renal pelvis was dilated obviously and filled with anechoic content (Fig. 2). The right kidney had decreased in echogenicity than pre-operative kidney.

Group III: Ultrasonography of the left kidney showed the renal cortex as a granular hypoechoic structure which was easily distinguished from the renal meulla. The renal medulla lost its lobulation and was visualized as a large anechoic centrally located structure which created distal acoustic enhancement (Fig. 3). The right kidney showed an increase in echogenicity in some areas of renal parenchyma. The urinary bladder appeared sonographically as anechoic structure outline by echogenic lines.

Group IV: Ultrasonography of the left kidney showed that the kidney as fluid filled sac. It was imaged sonographically as ovoid anechoic structure enclosed within echogenic wall. echogenic septa (arcuate vessels) appeared emerging from the wall to the anaechoic structure (Fig. 4). Ultrasonography of the right kidney showed a slight increase in the cortical echogenicity than in the sonogram of preoperative conditions.

Ultasonographic measurement's finding

Left kidney: As shown in Table 1, there were significant increases in the left kidney height ($p<0.05$) and renal medulla ($p<0.05$) at day 2. At day 7, the kidney width ($p<0.05$) and renal pelvis ($p<0.01$) were significantly increased.

There were no significant variation during the experiment period for the kidney length, ellipse and cortex starting from day 2-17 compared with day 0. At day 21, the results revealed significant increases in kidney length ($p<0.01$), width ($p<0.01$), height ($p<0.05$), ellipse ($p<0.01$), medulla ($p<0.05$) and renal pelvis ($p<0.05$).

Right kidney: Ultrasonographic measurements of right kidney length, width, height, ellipse, medulla, cortex and renal pelvis revealed no significant changes (Table 2).

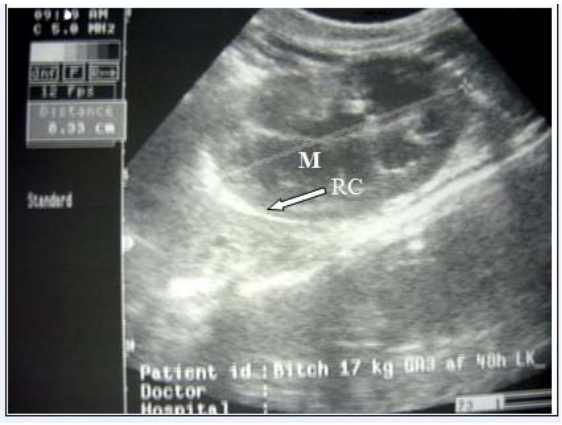

Fig. 1: Sagittal sonogram of Left Kidney (LK) at say 2 showing: enlarged anechoic Medulla (M), echogenic inter-lobar vesseles, echogenic corticomedullary junction, echogenic Renal Capsule (RC)

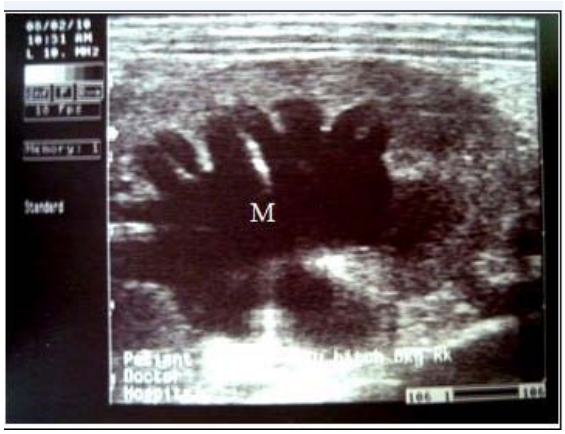

Fig. 2: Sagittal ultrasonographic image of LK by linear transducer at day 7 showing marked enlarged anechoic renal Medulla (M), granular hypoechoic renal cortex (C), short echoic inter-lobar vesseles, marked ehogenic corticomedullary junction, echogenic Capsule (RC) and distinct distal acoustic enhacement

Haematological and biochemical finding

Group I: Comparing data from day 0 with data at day 2 revealed insignificant changes in erythrocyte picture (Table 3), total leucocytes ($p<0.05$) and neutrophils ($p<0.01$) counts were significantly increased with insignificant changes in other leukocytic cells (Table 4). Serum biochemical constituents revealed no significant changes (Table 5).

Group II: No significant changes were observed in erythrocytes picture on days 3 and 7 (Table 3). There were

significant increases in total leucocytes and neutrophils counts on days 3 and 7. Lymphocytes count was significantly increased ($p<0.05$) at day 7 only (Table 4). Blood urea nitrogen showed significant increases at day 3 ($p<0.01$) and day 7 ($p<0.05$). There were a significant increase ($p<0.05$) in serum creatinine at day 7 and significant decrease ($p<0.01$) in serum creatinine clearance at day 7 (Table 5).

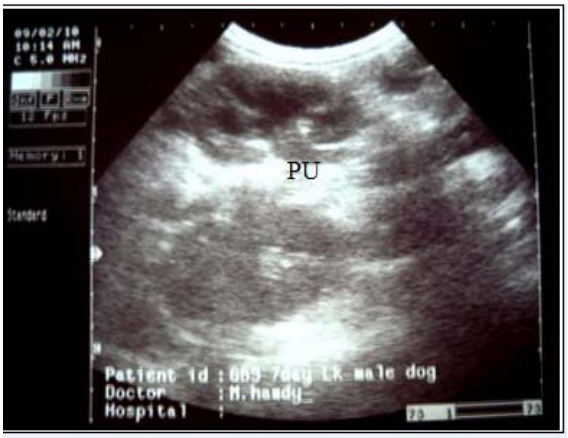

Fig. 3: Transverse sonogram of LK at day 14 showing enlarged anechoic Renal Pelvis (RP) and Left Ureter (LU)

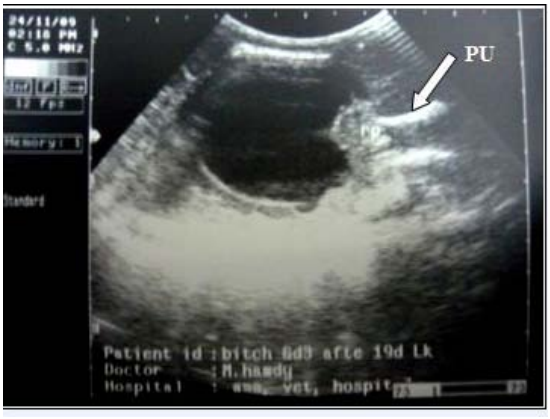

Fig. 4: Transverse sector scanned sonogram of LK at day 21 showing the kidney as anechoic fluid filled sac with severe distal enhancement and enlarged anechoic Proximal Ureter (PU)

Group III: There were significant decreases ($p<0.01$) in total RBCs count and PCV% at day 14 after ureteral ligation, associated with insignificant changes in mean corpuscular values indicating a normocytic normochromic anaemia (Table 3). Total leucocytes count was significantly increased at day 10 ($p<0.01$) and day 14 ($p<0.05$), lymphocytes and neutrophils counts showed significant increases ($p<0.05$) at day 10 only (Table 4). Serum creatinine clearance showed a significant increase at day 14 (Table 5).

Group IV: There were no significant changes in erythrocyte picture (Table 3). Total leucocytes and neutrophils counts were significantly increased at Day 17, with insignificant increases at day 21. Eosinophils count was significantly decreased at day 17 compared with day 0 and 21 (Table 4). Blood urea nitrogen showed significant increases at day 17 ($p<0.01$) and day 21 ($p<0.01$). In addition, serum creatinine was significantly increased at day 17 ($p<0.01$) (Table 5).

Histopathological findings: Group I: In animals belong to group I, there were no variation in size between right and left kidney (Fig. 5). Microscopic examination of the left kidney revealed glomerular swelling and congestion (Fig. 6). Edema in the interstitium and mild degenerative changes in the renal tubules were observed.

Group II: The left kidneys were larger than right ones (Fig. 5). Microscopic examination of the left kidney revealed vacuolation of the renal tubular epithelium and swelling of the glomeruli of most kidneys. Right kidney showing enlarged and hypertrophy of the glomeruli (Fig. 6).

Group III: The left kidneys were larger than right ones (Fig. 5). Microscopic examination of the left kidney revealed vacuolation of the renal tubular epithelium which was the most frequently observed lesion. Some renal tubules showed simple tubular dilatation in which the

Table 1: Ultrasonographic measurements for left kidney before and after ureteral ligation in dogs

	Control		Group I		Group II		Group III		Group IV	
Measurements	Day 0	Day 21	Day 0	Day 2	Day 0	Day 7	Day 0	Day 14	Day 0	Day 21
Length (cm)	6.29±0.66	6.22±0.88	5.98±0.80	6.98±0.90	5.83±1.23	7.37±1.220	5.91±0.740	6.73±0.320	5.99±0.31	7.67±0.810**
Width (cm)	3.66±0.11	3.77±0.33	3.30±0.39	3.87±0.38	3.52±0.49	4.61±0.690*	3.73±0.420	4.31±0.360	3.56±0.32	5.22±0.730**
Height (cm)	3.36±0.35	3.33±0.50	2.83±0.45	3.57±0.35*	3.59±0.71	4.52±1.220	3.76±0.610	4.15±0.180	3.46±0.31	4.42±0.570*
Ellipse (cm)	23.45±4.82	25.65±9.27	18.89±2.39	27.19±7.00	24.85±6.98	46.91±30.07	27.39±11.06	44.48±11.76	20.12±5.76	72.16±20.48**
Medulla (cm)	0.92±0.13	0.81±0.06	0.80±0.14	1.09±0.08*	0.93±0.04	1.15±0.380	0.95±0.120	0.79±0.300	0.95±0.10	0.70±0.100*
Cortex (cm)	0.72±0.12	0.62±0.11	0.62±0.12	0.65±0.05	0.94±0.12	0.90±0.080	1.00±0.130	1.09±0.100	0.80±0.21	0.90±0.100
Renal pelvis (cm)	1.32±0.33	1.26±0.10	1.10±0.26	1.55±0.36	1.26±0.18	2.33±0.410**	1.52±0.310	2.03±0.460	1.16±0.24	2.25±0.750

Data expressed as mean ± SD, Significant Difference ($p<0.05$, **$p<0.01$)

Table 2: Ultrasonographic measurements for right kidney before and after ureteral ligation in dogs

	Control		Group I		Group II		Group III		Group IV	
Measurements	Day 0	Day 21	Day 0	Day 2	Day 0	Day 7	Day 0	Day 14	Day 0	Day 21
Length (cm)	6.28±0.63	6.18±0.59	6.06±0.58	5.95±0.86	6.51±0.760	6.56±0.990	6.03±0.53	6.17±0.86	5.87±0.26	6.13±1.08
Width (cm)	3.42±0.46	3.26±0.58	3.16±0.51	3.13±0.49	3.37±0.420	3.97±0.720	3.19±0.47	3.50±0.34	3.25±0.22	3.85±0.62
Height (cm)	2.88±0.32	3.17±0.56	2.89±0 49	3.09±0.47	3.41±0.700	3.35±0.760	3.69±0.27	3. 31±0.31	3.42±0.35	3.73±0.87
Ellipse	17.42±5.10	18.78±9.45	14.46±4.55	16.35±5.32	22.76±13.38	25.39±12.75	19.93±5.84	21.72±4.97	19.17±5.21	31.69±14.32
Medulla (cm)	0.78±0.10	.91±0.14	0.67±0.09	0.85±0.28	0.90±0.080	0.83±0.140	0.92±0.15	0.98±0.16	0.71±0.08	0.82±0.16
Cortex (cm)	0.77±0.15	.67±0.11	0.60±0.14	0.72±0.09	0.89±0.100	0.87±0.180	0.93±0.09	0.97±0.15	0.72±0.05	0.70±0.24
Renal pelvis (cm)	1.36±0.12	1.32±0.34	1.09±0.34	1.04±0.35	1.22±0.200	1.30±0.240	1.34±0.12	1.43±0.12	1.0 ±0.160	1.0±0160

Data expressed as mean±SD

Table 3: Erythrocyte picture in dogs before and after unilateral ureteral ligation

Measurements	Day 0	Day 2	Day 3	Day 7	Day 10	Day 14	Day 17	Day 21
Total RBCs count (10^6 mm^{-3})								
Control	7.10±0.800	8.7±2.50	6.9±1.10^a	7.0±1.1^a	6.59±1.100^a	6.67±1.33^a	7.10±0.890^a	7.10±0.930^a
Group I	7.00±0.700	7.9±1.80	-	-	-	-	-	-
Group II	8.80±1.500^a	-	8.6±1.40^a	8.8±0.3^a	-	-	-	-
Group III	9.60±1.700^a	-	-	-	8.26±0.780^{ab}	6.60±0.88^b	-	-
Group VI	6.70±1.400^a	-	-	-	-	-	5.68±1.360^a	5.02±1.720^a
Haemoglobin conc. (g dL^{-1})								
Control	16.40±0.500^a	16.1±2.00^a	15.5±2.30^a	14.4±1.6^a	15.66±1.990^a	15.13±1.99^a	15.87±2.110^a	16.42±2.260^a
Group I	13.00±3.200^a	14.5±2.90	-	-	-	-	-	-
Group II	16.30±1.300^a	-	16.5±1.90^a	16.7±1.7^a	-	-	-	-
Group III	15.50±1.800^a	-	-	-	14.67±94.00^a	13.62±1.83^a	-	-
Group VI	14.20±2.200^a	-	-	-	-	-	13.90±3.100^a	11.98±4.620^a
PCV (%)								
Control	51.50±4.500^a	58.5±1.90^a	54.7±7.40^a	51.0±4.8^a	50.25±3.860^a	46.5±11.38^a	47.50±6.900^a	47.30±6.720^a
Group I	47.50±6.700	52.0±5.80	-	-	-	-	-	-
Group II	56.30±2.900^a	-	53.7±7.00^a	50.5±5.1^a	-	-	-	-
Group III	52.30±3.800^a	-	-	-	46.50±5.500^{ab}	43.25±2.75^b	-	-
Group VI	41.10±7.000^a	-	-	-	-	-	42.07±18.44^a	34.52±16.06^a
MCV (fl)								
Control	72.40±5.600^a	70.7±17.7^a	79.5±11.7^a	73.1±6.8^a	77.65±12.25^a	69.24±8.31^a	66.82±2.530^a	66.45±1.610^a
Group I	67.20±8.400	68.2±19.5	-	-	-	-	-	-
Group II	64.80±8.300^a	-	62.8±3.80^a	57.4±4.4^a	-	-	-	-
Group III	56.20±13.43^a	-	-	-	56.52±7.040^a	66.23±8.05^a	-	-
Group VI	61.60±8.500^a	-	-	-	-	-	68.67±15.99^a	65.03±9.240^a
MCH (pg)								
Control	23.20±2.500^a	19.3±4.40^a	22.6±3.90^a	20.7±1.8^a	24.05±3.600^a	22.97±2.50^a	22.80±0.600^a	23.10±0.420^a
Group I	18.70±5.700	18.8±4.80	-	-	-	-	-	-
Group II	18.80±2.600^a	-	19.8±5.40^a	19.0±2.1^a	-	-	-	-
Group III	16.63±4.150^a	-	-	-	17.88±2.040^a	20.67±1.52^a	-	-
Group VI	21.20±1.900^a	-	-	-	-	-	24.86±5.710^a	22.68±1.830^a
MCHC (g dL^{-1})								
Control	32.20±3.600^a	27.5±3.10^a	28.8±5.8^{0a}	28.4±2.2^a	31.08±2.000^a	33.46±4.90^a	34.22±0.730^a	34.80±0.240^a
Group I	27.50±5.600	28.3±7.00	-	-	-	-	-	-
Group II	29.00±2.100^a	-	31.3±6.90^a	33.5±6.1^a	-	-	-	-
Group III	29.94±5.100^a	-	-	-	31.92±4.530^a	31.48±3.66^a	-	-
Group VI	34.90±5.900^a	-	-	-	-	-	36.57±5.150^a	34.45±3.560^a

Data expressed as mean±SD, Significant Difference (*p<0.05). In each row, value followed by different letter are significant

tubular lumen increased in size and the tubular epithelium was normal in appearance. Atrophy of renal glomeruli and periglomerular fibrosis were frequently observed (Fig. 6).

Group IV: Left kidneys were larger in size than the right one (Fig. 5). In most cases, some renal tubules were atrophic and others were severely cystically dilated. The cyst cavity was lined by much flattened epithelium. Severe degeneration and vacuolation of the renal tubules were also observed in some cases. Glomerular atrophy was constant finding in most kidneys which was characterized by shrinkage and contraction of glomerular tuft with dilatation of the bowman's space (Fig. 6). Unilateral complete or partial hydronephrosis may remain silent for long periods, since the unaffected kidney can maintain adequate renal function. Sometimes, its existence first becomes apparent in the course of intravenous pyelography. It is regrettable that this disease tends to remain asymptomatic, recognition of urinary obstruction is important because it increase the susceptibility to infection and to stone formation and unrelieved obstruction always leads to permanent renal atrophy.

Table 4: Leucocytes picture in dogs before and after unilateral ureteral ligation

Measurements	Day 0	Day 2	Day 3	Day 7	Day 10	Day 14	Day 17	Day 21
Total WBCs count a (10^3 mm^{-3})								
Control	17.20±3.85	24.76±1.36	25.72±4.47^a	24.00±7.08^a	15.71±5.60^a	17.76±5.10^a	20.15±7.980^a	21.33±7.63
Group I	18.57±8.13	30.05±2.86*	-	-	-	-	-	-
Group II	9.51±2.43^a	-	22.02±9.90^b	25.8±10.04^b	-	-	-	
Group III	10.99±2.42^a	-	-	-	21.80±4.83^b	19.46±6.86^b	-	-
Group VI	8.80±1.51^a	-	-	-	-	-	29.45±15.87^b	19.07±14.15^{ab}
Lymphocytes count (10^3 mm^{-3})								
Control	3.59±1.52	3.35±1.12	7.39±4.68^a	4.41±0.57^a	3.92±2.72^a	5.92±2.70^a	5.53±3.640^a	4.08±1.50^a
Group I	5.56±3.14	3.03±0.67	-	-	-	-	-	
Group II	2.68±0.55^a	-	2.57±0.36^a	4.50±1.64^b	-	-	-	
Group III	2.03±0.51^a	-	-	-	3.47±0.67^b	3.26±1.25^{ab}	-	
Group VI	2.51±1.52^a	-	-	-	-	-	2.58±2.360^a	2.72±1.67^a
Neutrophils count (10^3 mm^{-3})								
Control	12.0±5.160	17.85±9.54	14.75±7.68^a	16.00±5.55^a	9.29±4.30^a	9.65±2.83^a	14.59±6.700^a	17.81±0.64^a
Group I	9.17±4.19	21.09±1.34**	-	-	-	-	--	-
Group II	5.21±1.97^a	-	16.59±7.96^b	16.50±8.51^b	-	-	-	-
Group III	7.50±2.35^a	-	-	-	16.48±4.94^b	14.20±7.13^{ab}	-	-
Group VI	5.02±1.89^a	-	-	-	-	-	24.42±1.680^b	13.78±12.6^{ab}
band cells count (10^3 mm^{-3})								
Control	0.17±0.16	1.19±1.33*	1.05±0.88^a	1.09±0.38^a	0.42±0.36^a	0.45±0.23^a	-	1.03±0.47^a
Group I	0.19±0.09	0.58±0.31	-	-	-	-	0.41±0.320^a	-
Group II	0.19±0.16^a	-	0.63±0.36^a	1.36±1.30^a	-	-	-	-
Group III	0.10±0.06^a	-	-	-	0.22±0.05^a	0.25±0.09^a	-	-
Group VI	0.038±0.3^a	-	-	-	-	-	2.44±2.330^a	1.13±1.10^a
Eosinophils count (10^3 mm^{-3})								
Control	1.22±0.55	1.52±0.77	1.39±0.44^a	0.78±0.38^a	1.35±0.51^a	1.06±0.69^a	0.43±0.330^a	1.08±0.91^a
Group I	2.03±0.57	2.77±1.56	-	-	-	-	-	-
Group II	0.85±0.28^a	-	0.94±0.78^a	0.62±0.51^a	-	-	-	-
Group III	0.38±0.30^a	-	-	-	0.51±0.38^a	0.89±0.63^a	-	-
Group VI	0.69±0.42^a	-	-	-	-	-	0.0^b	0.76±0.55^a
Monocytes counts (10^3 mm^{-3})								
Control	0.20±0.16	0.83±0.15	1.24±1.02^a	1.71±1.11^b	0.67±0.20^a	0.65±0.49^a	0.78±0.500^a	1.31±0.91^a
Group I	1.61±0.71	2.56±0.38	-	-	-	-	-	-
Group II	0.72±0.53^a	-	1.28±0.87^a	1.49±0.72^a	-	-	-	-
Group III	0.88±0.29^a	-	-	-	1.11±0.47^a	0.65±0.33^a	-	-
Group VI	0.48±0.40^a	-	-	-	-	-	0.0	0.68±0.67^a

Data expressed as mean±SD, Significant Difference (*p<0.05). In each row, value followed by different letter are significant

Table 5: Serum biochemical constituents in dogs before and after unilateral ureteral ligation

Measurements	Day 0	Day 2	Day 3	Day 7	Day 10	Day 14	Day 17	Day 21
BUN (mg dL^{-})								
Control	12.40±7.80	9.3±2.90	7.70±1.35^a	13.32±1.65^a	9.94±2.36^a	11.93±5.33^a	8.55±4.400^a	13.42±4.260^a
Group I	6.50±0.10	15.7±7.60	-	-	-	-	-	-
Group II	10.30±3.30^a	-	22.03±7.86^b	18.38±2.05^b	-	-	-	-
Group III	9.78±2.68^a	-	-	-	10.16±2.45^a	11.35±3.34^a	-	-
Group VI	9.59±0.60^a	-	-	-	-	-	40.07±28.94^b	40.57±15.31^b
Creatinine (mg dL^{-})								
Control	1.10±0.40	1.1±0.40	1.09±0.15^a	1.35±0.22^a	1.27±0.33^a	1.03±0.31^a	0.99±0.100^a	1.06±0.100^a
Group I	1.30±0.60	1.7±0.20	-	-	-	-	-	
Group II	0.90±0.10^a	-	1.73±0.44^{ab}	2.03±0.67^b	-	-	-	-
Group III	1.33±0.11^a	-	-	-	1.53±0.59^a	1.02±0.60^a	-	-
Group VI	0.78±0.16^a	-	-	-	-	-	1.28±0.310^b	0.75±0.180^a
Total protein (g dL^{-})								
Control	6.30±1.30	6.1±0.40	6.84±1.34^a	7.22±0.68^a	6.96±0.90^a	6.88±0.84^a	6.11±1.150^a	6.51±1.370^a
Group I	5.80±1.00	5.4±0.60	-	-	-	-	-	-
Group II	6.60±0.60^a	-	6.56±1.52^a	6.85±1.54^a		-	-	-
Group III	6.03±1.45^a	-	-	-	6.39±0.91^a	8.10±1.78^a	-	-
Group VI	8.26±1.98^a	-	-	-	-	-	7.65±1.860^a	7.35±0.310^a
Albumin (g dL^{-})								
Control	2.30±0.20	2.4±0.04	2.87±0.78^a	2.38±0.30^a	2.55±0.37^a	2.82±0.69^a	2.76±0.600^a	2.36±0.500^a
Group I	2.50±0.40	2.8±0.10	-	-	-	-	-	-
Group II	3.09±0.40^a	-	2.47±0.36^a	2.49±0.56^a	-	-	-	-
Group III	3.32±0.56^a	-	-	-	2.61±0.35^a	2.64±0.60^a	-	-
Group VI	2.36±0.55^a	-	-	-	-	-	2.66±0.510^a	2.50±0.490^a
Globulin (g dL^{-})								
Control	3.90±1.30	3.4±0.60	3.96±0.76^a	4.83±0.56^a	4.41±1.09^a	4.00±0.92^a	3.35±0.660^a	4.14±1.750^a
Group I	3.10±0.90	2.6±0.60	-	-	-	-	-	-
Group II	3.54±0.47^a	-	4.08±1.21^a	4.35±2.05^a	-	-	-	-

Table 5: Continue

Measurements	Day 0	Day 2	Day 3	Day 7	Day 10	Day 14	Day17	Day21
Group III	2.71±0.89[a]	-	-	-	3.77±.69[ab]	5.45±1.53[b]		
Group VI	5.89±1.71[a]	-	-	-	-	-	4.99±1.46[a]	4.85±0.56[a]
Creatinine clearance (mL min^{-1})								
Control	32.96±19.58	-	-	-	-	-	-	27.27±13.65
Group I	16.70±5.10	12.4±2.9	-	-	-	-	-	-
Group II	32.85±9.37	-	-	13.56±5.19**	-	-	-	-
Group III	19.51±1.79	-	-	-	-	27.61±5.93*	-	-
Group VI	24.87±9.48	-	-	-	-	-	-	23.91±9.08

Data expressed[a]s mean±SD. In each row, value followed by different letterare significant

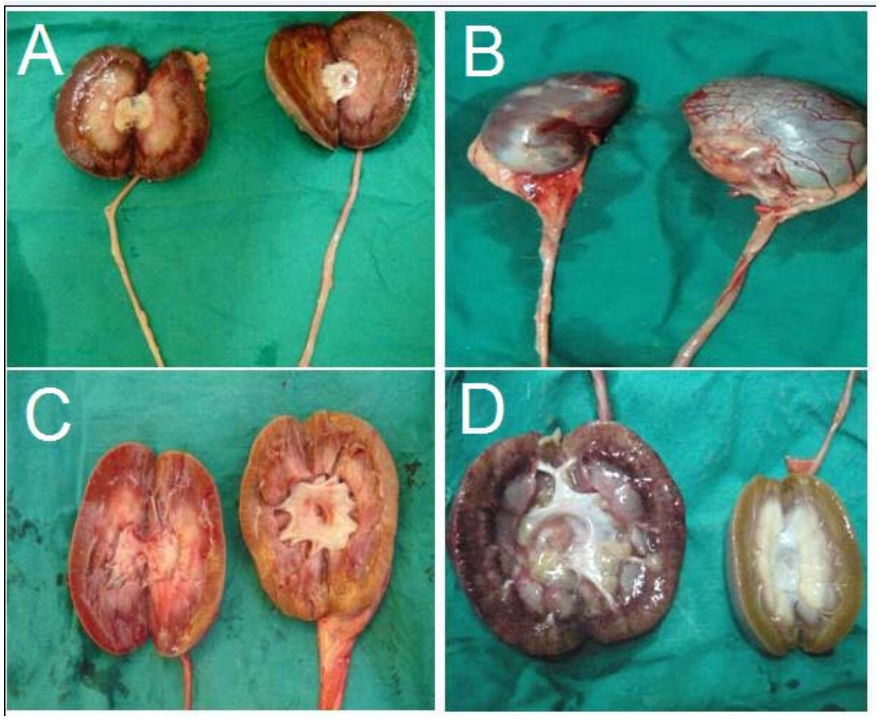

Fig. 5: Gross pathological changes in the kidneys of dog after unilateral ureteral ligation; A. (group I): No variation of size between right and left kidney, left kidney is paler than right; B. (group II): Left kidney severely congested; C. (group III): The left kidney enlarged than right one. The left kiney pale on cut section; D. (group IV): Left kidney appear enlarged, congested and elarged renal pelvis

The significant decreases ($p<0.01$) in total RBCs count and PCV% at day 14 might be attributed to the decrease synthesis of erythropoietin by the atrophied glomeruli which affect the synthesis of RBCs from the bone marrow and results in normocytic normochromic anaemia (Guyton and Hall, 1998).

The significant increase in total leucocytes and neutrophils counts during the period from day 2-17 may be attributed to the inflammatory reaction produced by traumatized tissues at the site of surgical operation and at the site of ureteral ligation. Serum biochemical changes observed after ureteral ligation may be attributed to the degenerative changes occurred in the kidney that drained by the legated ureter (left kidney). At day 2, significant serum biochemical changes were not found and at the same time significant ultrasonographic findings were observed. On days 3 and 7, the left kidney developed degenerative changes, severe congestion and swollen glomeruli which reflected on the blood as significant increases in serum BUN level on days 3 and 7 and significant increase in serum creatinine level ($p<0.01$) at day 7, another factor contribute in the increase of these toxic metabolites in the blood is the reduction in glomerular filtration of the healthy kidney which was confirmed by the significant decreases in serum creatinine clearance ($p<0.01$). It was stated that serum concentration of markers of renal function (urea and creatinine) rise when the rate of production of metabolic waste exceeded the rate of renal excretion (Abuelo, 2007).

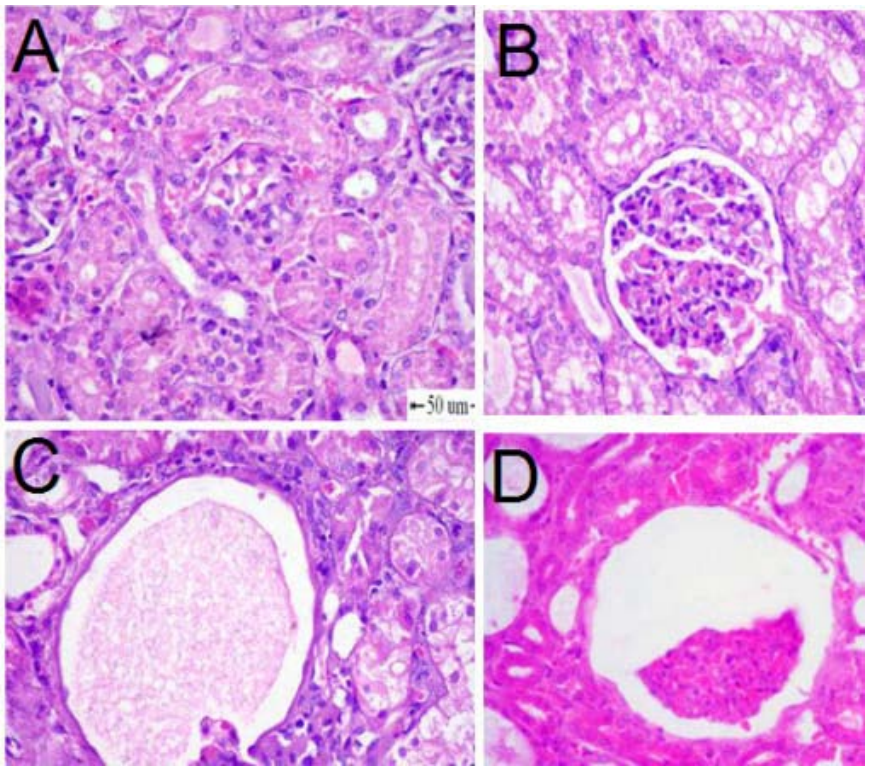

Fig. 6: Representative micrographs for some pathological changes in the kidneys of dog; A. (group I): Kidney showing glomerular swelling and congestion; B. (group II): Kidney showing vacuolar degeneration and swollen glomeruli; C. (group III): Glomerular atrophy and periglomerular fibrosis and D. (group IV): Atrophy of glomeruli H&E stain

The current study may prove the efficacy of the ultrasound in detecting the early renal changes at day 2. Marked hydrouretronephrosis was detected sono- graphically at day 7 as marked dilatation of renal medulla, renal pelvis, slight degree of atrophy of the renal cortex and proximal uerter dilatation. Inspite of these renal changes the animals had no observed clinical symptoms.

Day 14 represents the start of irreversible changes in the left kidney and the start of the compensatory changes of the right kidney as indicated by the increase of glomerular filtration rate but the compensatory mechanism for the healthy kidney was not well functioning till day 21 as serum blood urea nitrogen significantly increased on days 17 ($p<0.01$) and 21 ($p<0.01$).

In addition, serum creatinine was significantly increased ($p<0.01$) at day 17. The highest increases in these toxic metabolites were observed on days 17 and 21 which agreed with the irreversible changes detected by the histopathological and ultrasonographic examination of the legated kidney.

In the present study, the histopathological lesions ranged from mild degenerative changes in the renal tubules at day 2 to severe atrophy of the glomeruli, tubules and cystic dilatation of the renal tubules 3 weeks after legation.

These results are in agreement with previous studies (Sahal *et al*., 2005). Conclusively, the histopathological changes observed on days 14 and 21 indicated irreversible changes due to the glomerular atrophy and severe atrophy and dilatation of the tubules. While, the histopathological changes observed on days 2 and 7 may be considered reversible.

The biochemical changes were in harmony with the histopathological and ultrasonographic findings. The serum creatinine reached the maximum value at day 7 then decreased gradually till reach the lowest value at day 14. This may indicate that the time of maximum renal changes of the obstructed kidney was the same time for initiation of compensatory changes in the contra lateral sound kidney at day 7. The compensatory changes increased gradually till day 14 at which the sound kidney was able to get ride of waste products in blood specially the creatinine. Braun *et al*. (2003) reported a similar explanation. In conclusion, serum creatinine was the highest on days 3 and 7 while the creatinine clearance was

the lowest at day 7. The serum BUN was the highest at day 21. The major histopathological changes were observed at day 21, these changes were compatible with the ultrasonographic and biochemical findings.

CONCLUSION

In this study, serum creatinine was the highest on days 3 and 7 while the creatinine clearance was the lowest at day 7. The serum BUN was the highest at day 21. The major histopathological changes were observed at day 21, these changes were compatible with the ultrasonographic and biochemical findings.

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