

## **SUMMARY**

of the doctoral thesis entitled:

### **RESEARCH ON THE CLINICO-PATHOGENIC AND DIAGNOSTIC DOMINANTS OF SOME HEPATO-RENAL DISEASES IN CARNIVORES**

Ph.D-student: **ION Camelia Ramona**

Scientific coordinator: **Professor, PhD CODREANU Mario**

**KEYWORDS:** *canine, feline, hepato-renal disease*

The PhD thesis, entitled ***Research on the clinico-pathogenic and diagnostic dominants of some hepato-renal diseases in carnivores***, is structured in accordance with current provisions, and thus comprises two main parts:

-Part I corresponds to the bibliographical study associated with it and comprises 40 pages, representing 23,0 % of the thesis volume.

-Part II presents the own research and comprises 134 pages, representing 77,0 % of the thesis.

The research work was carried out between 2018-2022, at the Faculty of Veterinary Medicine Clinic Bucharest, Canivet Veterinary Practice and VetMedical Consulting SRL.

Hepato-renal disorders occupy a significant place in veterinary practice, given the polymorphism of etiopathogenetic factors and the variety of clinical signs observed, emphasizing the need for a statistical and detailed approach to these associated disorders. The diversity of the clinical manifestations, varying in intensity from one individual to another, as well as the pathophysiologic consequences affecting the hepato-renal system and the general homeostasis of the organism, emphasize the complexity and specificity of these disorders.

**Chapter I** of the first part of the thesis focuses on the morpho-physiologic peculiarities of the hepatic and renal system in carnivores, with their specific and comparative approach.

**Chapter II** of the first part of the bibliographic study of the thesis presents the clinical-pathogenetic framework in the main hepato-renal diseases in carnivores, with a brief presentation of the dominant clinico-pathogenetic features in hepatopathies and nephropathies in carnivores, approached by etiologic triggering factor, respectively inflammatory, degenerative, toxic, cystic and neoplastic.

**Chapter III** of the introductory part of this paper deals with the clinical-pathogenetic framework in the main parasitic hepato-renal disease-inducing conditions represented by anaplasmosis, erlichiosis, lyme disease, dirofilariasis and babesiosis.

The hepato-renal system plays an essential role as the first line of defense against the aggression of various etiologic agents. The liver, having detoxification, metabolism and synthesis functions, processes and neutralizes toxic substances in the body, including drugs, toxins and metabolic products. The kidneys, in turn, filter the blood, removing wastes and maintaining fluid and electrolyte balance. Together in a collaborative system they help maintain homeostasis and protect the body from the harmful impact of infections, toxins and metabolic stress. Consequently, any dysfunction of the hepato-renal system can have serious consequences for the overall health of the body, highlighting the importance of monitoring and maintaining the morpho-functional integrity of these vital organs.

The implementation of a rigorous medical screening, which includes thorough documentation of the patient's clinical status by centralizing physiological, biochemical and hematological data, together with information obtained by ultrasonographic, necropsy and cytological/histopathological investigations, is an essential method. It allows the clinician to exercise greater control in the management of disease, providing a sound basis for accurate diagnosis and effective therapeutic interventions.

**Part II** of the dissertation, entitled "**Personal Research**", constitutes approximately 80% of the total dissertation and is organized in 3 chapters, general conclusions and bibliography. The results of this work are exemplified through tables, graphs and figures.

The first chapter of Part II, "**Clinical-diagnostic correlations in carnivore hepatopathies**", highlighted the diagnostic process in a total of 283 dogs and 226 cats totaling 509 carnivores.

**Acute hepatitis** was diagnosed in 27.2% (n=77), which were evaluated in dynamics by paraclinical and ultrasonographic analysis a total of 8 canids (10.4%).

The symptomatology recorded by the data collected from the owners and the data recorded on clinical examination summarize the presence of hepatoencephalic syndrome in 3 canines with a percentage of 37.5%, digestive syndrome with repeated vomiting and diarrhea in 87.5%, (n=7), jaundice in 4 dogs (50.0%) and disseminated intravascular coagulation in 12.5% of canines (n=1), abdominal tenderness in 87.5%, (n=7) and fever in 8 dogs (100%).

Collected biochemical data captured from the fully investigated cases increased above normal parameters of ALT, in particular, with mean value of 355 (U/I), AST - mean value of 97 (U/I), ALP in the value of 288 (IU/L), and ammonia in patients with hepatic encephalopathy, reduced urea in 6 patients, hypoglycemia in 2 individuals, hypoproteinemia in all evaluated patients, and neutrolytic hemoleukograms in all included patients, accompanied by thrombocytopenia in 8 dogs.

Acute feline **cholangiohepatitis** was diagnosed in 41 felines that showed a clinical picture characteristic of acute liver involvement, being in agreement with previous studies, namely fever, anorexia, lethargy, digestive syndrome and jaundice, appreciated in dynamics by paraclinical and ultrasonographic data with a diagnosis of certainty in a total of 11 felines (26.8%).

The centralized clinical manifestations summarize the presence of febrile syndrome in 9 cats (81.8%), vomiting in 63.6% (n=7), diarrhea in 3 cats (27.3%), jaundice in 4 cats (36.4%) and non-specific signs of anorexia, weakness and lethargy in all patients.

The biochemical profile showed elevations in serum transaminases, with an impressive increase in ALT in all felines, hyperbilirubinemia in 6 cats (54.5%) and leukocytosis in 11 individuals.

**Chronic hepatitis and liver cirrhosis** were diagnosed in 31.4% of the canids (n=89), of which a total of 14 canids (15.7%) were followed up in dynamics by repeated paraclinical determinations and clinical examinations.

The duration of illness ranged from 7 to 20 days, with various clinical manifestations, represented by inappetence (n=14), halitosis (n=11), melena (n=9), hematochezia (n=2), polyuria-polydipsia syndrome (n=13), dehydration (n=14), jaundice (n=12), weight loss (n=14) and abdominal distension.

Anemia was identified in all cases (100%), thrombocytopenia was detected in 6 cases (42.9%) and thrombocytosis in 2 patients (14.3%).

As for the leukocyte formula, neutrophilia was noted in 11 individuals with left shift of Arneeth index (78.6%), on the background of chronic hepatitis, which recorded neutrophilic leukocytosis. The final analysis of transaminases showed increased ALT, AST, ALP, creatinine, PT, GGT and total bilirubin. Hypoproteinemia is the most common abnormality in chronic disorders, as the liver is the main site of protein synthesis and degradation, an aspect also identified in our study.

**Hepatic steatosis** was found in 6 canids (2.1%), who clinically expressed non-specific symptoms, with a history of pancreatitis (n=1), chronic enteritis accompanied by prolonged anorexia (n=3) and as a result of porto-systemic shunt (n=2).

Symptomatology related to the centralized clinical data shows a neurological form in 5 individuals, with muscle weakness, ataxia, somnolence, convulsions, opisthotonus and coma in the last stage and 1 clinical case with symptoms related to diabetes mellitus associated with hepatic encephalopathy syndrome.

The paraclinical diagnoses include inconstant elevation of transaminases (n=6), hypoglycemia in 5 patients (83.3%), hyperglycemia in 16.7% of them (n=1) and hyperbilirubinemia (n=5).

**Hepatosteatosis** of the liver was diagnosed in 34 of the felines (15.0%), who presented to the clinic with prolonged anorexia and an impairment of general condition, with a diagnosis of certainty by paraclinical interventions being associated with a diagnosis in 13 felines (38.2%).

The lack of clinical lesions made the diagnosis difficult, as hepatic steatosis was clinically dominated by prolonged anorexia and in special situations hepatic encephalopathy was found, thus the presence of absolute anorexia over a long period was recorded in all cats included in the study and additionally, weakness (n=11), jaundice (n=9) and hepatomegaly were found in 7 cats (53.8%).

The most consistent laboratory findings were the presence of Heinz bodies, mild anemia in 4 individuals (30.8%), hyperbilirubinemia in 9 patients (69.2%), hypoalbuminemia and increases in serum ALP activity in 6 felines (46.2%) and GGT within normal limits.

**Poisoning with acute liver damage** in canids was recorded in 42 patients (14.8%), in whom classic symptoms of acute liver failure were detected, of which 23 canids (54.8%) were evaluated in dynamics and by complementary diagnostic methods.

Collected anamnestic data indicated hepatotoxicity due to xylitol poisoning (n=2), antifreeze (n=7), human drugs (n=6), veterinary drug overdose (n=3), toxic plants (n=2), grape consumption (n=1) and chocolate/theobromine consumption (n=2).

Clinical expressions with a dominant character, recorded in the animals included in the research by assuming a predominantly digestive symptomatology, altered general condition (n=21), anorexia (n=23), repeated bilious vomiting (n=23), yellow/hemorrhagic diarrheal stools (n=4), specific character - jaundice of different degrees of intensity manifested by 18 individuals, neurological symptoms included in hepatoencephalic syndrome (n=7), oliguria/anuria in 8 individuals, with specificity for renal co-infection.

The hematologic and biochemical profile is diverse due to the multitude of systemic pathogenetic consequences and directly proportional to the ingested toxicant, with alterations in liver, kidney and glycemic functional parameters, thus it was recorded predominantly in cases of xylitol intoxication - hypoglycemia (n=5), in intoxication with antifreeze/toxic plants/starches/chocolate - hypercreatinemia and hyperuremia in 11 cases, associated with acute renal impairment, elevated transaminases in 23 canines, mild anemia in 4 individuals and hyperbilirubinemia in 18 patients, with elevated ammonia in 7 dogs.

**Intoxications with acute liver** involvement in felines were recorded in 47 patients (20.8%), with 26 felines (55.3%) being dynamically evolutionarily appreciated.

Collected anamnestic data summarize the etiology and type of poisoning as being caused by human drugs (n=9), veterinary drug overdose (n=3), toxic plants (n=8) and antifreeze (n=6).

By centralizing the symptomatology, the presence of digestive disorders, namely repeated vomiting with bilious character (n=24), diarrhea with reduced frequency (n=3), anorexia (n=26), jaundice with different degrees of intensity expressed by 21

individuals, oliguria/anuria in 10 individuals, in correlation with renal impairment and neurological symptoms associated with hepatoencephalic syndrome (n=4).

The biochemical data show diverse changes due to the multitude of hepato-renal systemic pathogenetic consequences that are directly proportional to the ingested toxicant and the respective quantity, thus, liver transaminases were increased in 26 feline patients, hypercreatinemia and hyperuremia in 18 cases, associated with acute renal damage and hyperbilirubinemia in 21 feline patients, with increased ammonia in 2 cats.

**Hepatic neoplasms** were recorded in 69 canidae (24.4%), presented with digestive symptoms, with inappetence, polyuria-polydipsia syndrome, jaundice, anemia, biochemical-hematologic changes and ascites under the aspect of general liver failure syndrome, a total of 28 canidae (40.6%) were evaluated in dynamics.

The prevalence of neoplastic hepatopathies registers in the Metis breed the percentage of 14,3 % (n=4), Shi-Tzu in number of 9 (32,1 %), German Shepherd with the percentage of 7,1 % (n=2), Yorkshire Terrier with the percentage value of 21,4 % (n=6) and Peckinez breed 25, 0 % (n=7), 9 males (32.1 %) and an increased representation of females with a percentage of 67.9 % (n=19), attributed to the increased incidence of liver metastasis following mammary carcinoma.

The diagnosis was often a surprise on ultrasonography, especially in focal lesions, while diffuse lesions had obvious clinical determinism, represented by inappetence/anorexia (n=26), polyuria-polydipsia syndrome (n=11), dehydration (n=15), jaundice (n=9), weight loss (n=28) and abdominal distension (n=6)

Abnormalities in the initial hematologic or biochemical profiles are minimal, with hyperrepresentation of transaminases, particularly AST, hypoglycemia due to large tumor mass (increased glucose utilization) or paraneoplastic effect (insulin-like effect), aregenerative anemia and hyperbilirubinemia.

Hepatic neoplasms were recorded in 104 cats (46.0%) with general clinical symptoms of anorexia, lethargy, jaundice or asymptomatic course, with a total of 43 cats (41.3%) being evaluated in the dynamic.

An asymptomatic evolution was observed by single or focal lesions, unaccompanied by a clinical procession or non-specific clinical expression with altered appetite ranging from capricious appetite to absolute anorexia in 95.3% of the cats, (n=41), jaundice (n=21), weight loss (n=43), vomiting (n=36) and abdominal distension (n=8).

The hematologic or biochemical changes consisted of increased transaminases, ALT, AST, GGT, ALP, total cholesterol and total bilirubin, with aregenerative anemia and absence of an inflammatory response on the leukocyte formula.

**Chapter V** of the second part of the PhD thesis, entitled "*Clinico-diagnostic correlations in nephropathies in carnivores*" includes the clinico-paraclinical analysis in order to establish a final diagnosis of nephropathy in 482 carnivores, 134 dogs and 348 cats, respectively.

The dominant clinical manifestations in **nephritis**, dressed the general picture of acute systemic evolution translated by the presence of fever syndrome in 7 patients, together with apparent injected mucous, tachypnea and tachycardia, kyphosis/lumbago in 5 of them, exacerbation of renal painful tenderness on palpation of the lumbar area in 6 of the dogs, oliguria in 7 of the individuals, and urinary sediment examination showed the presence of hematomas, epithelial, granular, hematic cylinders and intense albuminuria in all patients included in the study.

The ultrasonographic report shows diffuse renal hypoechoechogenicity, nephromegaly and obliteration of the cortico-medullary ratio.

Of the total number of patients with nephritis diagnosed by clinico-paraclinical data, special necropsy examinations were performed in 3 cases who died as a consequence of systemic cortico-systemic injury caused by acute renal involvement, where specific lesions of interstitial nephritis were detected, namely focal congestion, adhesions at the level of the capsule with the renal parenchyma, smooth appearance in 2 cases and diffuse granular appearance in 1 case, with variable severity and distribution in one or both kidneys.

Of the patients who underwent macroscopic examination, the presence of the etiologic agent *Leptospira interrogans* was detected in 2 cases, and *Escherichia coli* in 3 cases, thus 18.2% of patients and 27.3% of patients had associated complex between PCR testing at a private clinic and histopathologic examination.

In felines, the diagnosis of inflammatory nephropathy captured the presence of pyelonephritis pathology being identified in 7 felines, presented to the clinic for general non-specific changes.

Dominant clinical manifestations observed in this study in felines include fever syndrome - present in 7 of the cats, kyphosis/lumbago observed in 7 of the cats, polydipsia polyuria syndrome - present in 5 of the cats, repeated vomiting - recorded in 4 of the cats, exacerbated painful tenderness on palpation of the kidneys - observed in 7 cats and the presence of hemocytes and leukocyturia on urinary sediment examination.

Ultrasonographic examination showed nephromegaly, diffuse hypoechoechogenicity and blurring of the cortico-medial demarcation, with ectaticity of the vascular system (color Doppler).

In the study, degenerative renal pathology in canids included a diagnosis of **renal amyloidosis** in 4 of the canids (3.0%).

By centralizing the prevalence data by breed, an increased prevalence in the Shar Pei breed of 75.0 % (n=3) was noted, which is correlated with published data from previous research, and 1 patient belonging to the Metis breed (25.0 %), with an average age of 4.5 years, was included in the 1-5 years age category.

The most common clinical signs exhibited by the canine population studied included anorexia (n = 4, 100%), vomiting (n = 3, 75%), lethargy (n = 4, 100%), polyuria and polydipsia (n = 3, 75%) and emaciation (n = 2, 50%).

The most frequent hematologic abnormalities in the canines studied included aregenerative anemia (75%) and leukocytosis (75%). Centralized biochemical data captured the presence of hypoalbuminemia in all canine patients, associated with a mean creatinemia of 5.5 mg/dL, serum uremia at a mean value of 87 mg/dL, hypocalcemia in 3 individuals, elevated transaminases in 2 patients, and proteinuria in all dogs included in the study.

Histopathologic examination - Typical reddish-pink colored amyloid deposits in the renal glomeruli at the glomerular arterioles with disappearance of normal glomerular tissue. Hemosiderosis due to renal interstitial hemorrhage. Replacement of glomerular tissue with edema, hemorrhage, and necrosis has been demonstrated in a large proportion of glomeruli. Vacuolization of the epithelium of the uriniferous tubules accompanied by intratubular edema and necrosis of the tubular epithelium.

**Poisoning with acute kidney damage** in canids was recorded in 41 patients (30.6%), in whom classic symptoms of acute renal failure were detected. The anamnesis collected from the owners indicated as triggering factors - antifreeze (n=7), human drugs (n=6), overdose with veterinary drugs (n=3), toxic plants (n=11), consumption of grapes (n=8), chocolate/theobromine (n=6) (Graph 5.14).

The predominant clinical symptoms observed in the animals included in the research were mainly renal in nature, through the manifestation of acute kidney injury syndrome. These included: altered general condition (n=41), anorexia/inappetence (n=41), vomiting (n=36), diarrhea (n=12), jaundice of varying degrees of intensity (n=18), neurologic impairment (n=9) and oliguria/anuria in all patients, all associated with renal impairment.

Alterations in renal functional parameters were predominant in cases of poisoning with antifreeze, toxic herbs, grapes and chocolate, manifesting as hypercreatinemia and hyperuremia in 41 cases. In addition, inconstant increases in transaminases were observed in 21 canids and severe aregenerative anemia in 18 individuals.

Ultrasonographic imaging of the kidney with oxalate nephrosis revealed ultrasonographic changes that ranged from mild to marked increase in renal cortical echogenicity with varying degrees of intensity of the corticomedullary junction (the "halo" sign) supporting presumptive ethylene glycol intoxication, along with ultrasonographically inconsistent features in intoxications of diverse origin with foci of necrosis appearing as regions of mixed or increased echogenicity, reflecting the degree of tissue damage.

**Poisoning with acute renal involvement** in felines was detected in 119 patients (34.2%), who showed predominantly symptoms characteristic of acute renal failure, with multifactorial etiology, being evaluated dynamically and exclusively in the clinic - 42 felines (35.3%).



Anamnestic data collected from the owners of the cats summarize the causes and types of poisoning as follows: human drugs (n=17), overdose with veterinary drugs (n=5), toxic plants (n=9) and antifreeze (n=11).

Recorded clinical data indicate a non-specific character by association with digestive disorders, namely repeated vomiting (n=38), diarrhea with low frequency (n=9), anorexia (n=42), jaundice with different degrees of intensity expressed by 14 individuals, and with indicative character for diagnosis - oliguria/anuria in 42 individuals.

The biochemical profile shows the renal impact of the toxins by increased serum creatinemia and uremia in affected patients, increased liver transaminases in 18 cases, with inconstant liver damage. Calcium oxalate crystals were detected in the urinary sediment, with specificity for the diagnosis of ethylene glycol intoxication.

Renal ultrasonography in cases of oxalate nephrosis showed variations in ultrasonographic changes, ranging from mild to a significant increase in renal cortical echogenicity. These changes, together with variations in the intensity of the corticomedullary junction (known as the 'halo' sign), support the hypothesis of possible ethylene glycol intoxication. In addition, variable ultrasonographic features have been observed in intoxications of various origins, including foci of necrosis appearing as regions of mixed or increased echogenicity, indicating the degree of tissue damage.

In the present investigation, cystic nephropathies were identified in 21 canids, with an incidence rate of 15.7%, which had a poorly representative or chronic course in the form of nitrogen retention syndrome.

**Solitary renal cyst** was discovered incidentally at routine annual examinations in 8 canids (29.82%), with no changes in physiologic parameters. In contrast, multiple cysts in the form of polycystic kidney disease was identified in 13 canines (38.1%) on the basis of specific clinical and paraclinical disturbances, which triggered chronic renal failure, along with all the clinical symptoms characteristic of this condition.

Ultrasonography allowed the identification of renal cysts, with the characteristic appearance of anechoic, round or ovoid structures, with a contour delimited by a thin and hyperechoic wall, which may generate posterior acoustic shadows.

In felines, the cumulative incidence per cases investigated revealed 14 single renal cysts (20.9%), and 53 felines (79.1%) were diagnosed with PKD (polycystic kidney disease). In the study, the Persian breed was found to have the highest incidence rate at 38.8% (26 affected felines).

Analysis of the general symptomatology observed in cats with polycystic kidney disease (**PKD**) shows a marked deterioration of general condition in 41 cats (61.2%), accompanied by a significant decrease in body index and marked weight loss. Dehydration was present in 79.1% of patients (n=53), reflecting the systemic pathogenetic consequences of CKD. The uremia-related symptomatology resulted in the presence of gastrointestinal disorders with anorexia observed in 67.2% (n=45),



frequent vomiting of various types - food, glerose or in the form of hematemesis in 61.2% of cases (n=41) and halitosis in 34 individuals (50.7%).

In addition to the general symptomatology, the presence of polyuria-polydipsia syndrome was observed in 79.1% of patients (n=53) and hypothermia in 31 cats (46.3%). These findings emphasize the severity and extent of symptoms among felines affected by PKD.

Specific changes in paraclinical investigations were observed in patients with chronic kidney disease (CKD), numbering 53 cases. These changes were also associated with the advanced age of the patients and wear-related pathologies.

In this thesis, we identified neoplastic nephropathy in 57 canids of different breeds and ages, which were brought to the veterinary practice for investigation after their owners observed overt clinical manifestations.

The clinical expressions (systemic and specific) included moderate to obvious clinical signs, correlated with renal neoplastic pathology or sclero-infiltrative phenomena related to old age, tenderness on the renal area - diffuse/increased in 22 of the patients, non-specific digestive disturbances as a result of uremic intoxication (halitosis, vomiting, anorexia, capricious appetite) in 96.5% of them (n=55), weakness in all affected patients, polyuria-polidippsia following the onset of nitrogen retention syndrome in 51 of the individuals (89.5%) and hypothermia in 33 of the canids (57.9%), in forms and degrees of severity associated with individual reactivity.

The metabolic disturbances at the biochemical level that support and indicate a moderate to severe renal dysfunction, with relevance in the diagnosis of chronic renal failure, were represented by serum creatinine level, serum urea, which recorded mean values of 6.9 mg/dL and 181 mg/dL, respectively, in addition to systemic changes represented by hypoproteinemia, inconstant increase in liver transaminases, and the assessment of hematological status highlights a clear tendency towards hyporegenerative anemia, in correlation with the morphological and substitutive alterations of the renal parenchyma.

**Renal tumors** were detected in 77 felines (22.1%), who presented with relatively nonspecific symptoms. The dominant clinical manifestations observed in the animals included in this study were predominantly of a digestive nature, highlighting the expression of individual differences. Thus, vomiting was present in 79.2% of the patients (n=61), and was associated with a diarrheal syndrome in 15.6% (n=12).

From the biochemical investigative ensemble conducted, the evaluation of creatinine activity was the most relevant for detecting renal impairment. In association with the levels of serum uremia, increases in these parameters were recorded, suggesting a deterioration of renal function.

In Chapter VI, "*Clinical-diagnostic correlations in conditions inducing hepatorenal diseases in carnivores*," the group of 81 canines clinically and paraclinically approached is presented, with a final diagnosis of anaplasmosis in 8

individuals, ehrlichia canis in 3 canines, dirofilariasis in 38 canine patients, Lyme disease in 2 confirmed cases, and babesiosis in 30 dogs.

In the present study, hepato-renal functional changes/co-affects (at the upper limit) caused by the etiological agents **Anaplasma phagocytophilum** and **Anaplasma platys**, with diagnoses established through the Snap Test 4DX, slide examination, and confirmed by positive PCR genetic testing, were detected in 8 canines. Clinical-anamnestic data provide an absolutely vital foundation for presuming a diagnosis, allowing for supplementation through paraclinical analyses with blood biochemistry and hematology.

During the clinical examination, a general state of apathy was noted in the affected patients, epileptiform seizures in 2 individuals (25.0%), along with the predominantly identified clinical sign of anemic mucous membranes in 7 canine patients included in the final study (87.5%).

The analysis of the biochemical and hematological profile reveals monocytosis (6/8), thrombocytopenia (5/8), with renal functionality impairment with an average creatinine of 2.11 mg/dL and inconsistent hepatic impairment through a relative increase in serum transaminases with an average of 111 U/L.

**Ehrlichiosis** was diagnosed in 3 canines out of the total patients tested for infectious-parasitic diseases, recording a low prevalence (3.7%).

A systemic analysis of the clinical coordinates indicates a lack of specific symptomatology, with general clinical data recorded represented by anemia and neurological impairment manifested by the expression of epileptiform-type seizures.

**Lyme disease** was diagnosed in 2 dogs out of the total number of patients evaluated for infectious-parasitic diseases, indicating a low prevalence of 2.5%. Clinically, the patients did not exhibit the specific symptoms of Lyme disease, but rather general clinical signs associated with chronic kidney disease.

**Heartworm disease** was identified in 38 dogs out of the total number of patients in the study (46.9%), reflecting a persistent health issue for this population. The collected statistics show the following percentages by age and sex for the affected dogs: in the age group of 1-5 years, 28.9% (n=11) of the cases are affected; in the age group of 6-10 years, there are 15 dogs; and in the age group of 11-17 years, 12 dogs are affected. Regarding sex distribution, male dogs represent 71.1% (n=27) of the total cases, and female dogs constitute 28.9% (n=11) of the recorded cases.

The overall clinical signs recorded in patients with heartworm disease include right-sided heart failure with changes in general condition in 97.4% of these cases (n=37), coughing manifested by 34 canine patients (89.5%), exercise intolerance in 81.6% of them (n=31), cyanosis in 11 dogs (28.9%), ascites and dyspnea in 42.1% (n=16), syncope (9/38), and collapse (9/38).

Additional clinical data highlight systemic involvement as a global consequence, evidenced by symptoms characteristic of liver failure in 9 individuals (23.7%) and a clinical picture consistent with azotemia in 7 dogs (18.4%).

As part of the established protocol, in addition to observing clinical manifestations, an integrated and correlated evaluation of changes in parameters associated with liver pathology was included. This specifically looked at serum transaminase levels, which exceeded the physiological range in 37.50% (n=9) of the cases, and elevated renal biochemical indicators in 7 of these dogs, along with leukocytosis in 10 dogs (26.3%), hyperglycemia in 5 dogs, lymphopenia in 2 dogs, thrombocytopenia in 6 dogs, and anemia in 5 dogs (13.2%).

**Babesiosis** was diagnosed in 30 dogs, who exhibited a characteristic clinical picture suggestive of parasitosis or a nonspecific progression discovered through paraclinical determinations.

The evaluation and outline of the clinical framework summarized the most important reported clinical manifestations, with a clinical picture corresponding to renal impairment in 8 individuals, a clinical ensemble characteristic of isolated liver impairment in 2 patients, a concomitant progression through dual hepatorenal systemic involvement in 6 dogs. Additionally, clinical data for babesiosis included febrile syndrome in 24 of them, hemoglobinuria in 27 canine patients, and jaundice in 9 individuals.

From the comprehensive biochemical and ultrasound investigation conducted, significant findings include thrombocytopenia in 13 dogs (43.3%), anemia in 9 dogs (30.0%), leukopenia in 9 animals (30.0%), thrombocytosis in 3 dogs (10.0%), and a leukocytic response in 2 cases (6.7%). Additionally, splenomegaly was identified in all patients included in the study, with PCR typing performed on 17 of them (56.7%).

Chapter X includes 216 bibliographical sources cited in the text.