



# Correlations Between Changes in Serum Cortisol Level and Biochemical Liver Profile and Adrenal Ultrasound Appearance in Hyperadrenocorticism (Cushing's Syndrome) in Dogs

## KEYWORDS

cortisol, transaminase activity, ultrasound changes, hyperadrenocorticism, dogs

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**ABSTRACT** *The purpose of this study was to establish an accurate and early diagnosis of hyperadrenocorticism in dogs, expressed mostly by Polyuria-Polydipsia syndrome, dorsal alopecia and abdominal ptosis, in accordance with the additional laboratory biochemical and hormonal changes, in order to establish the most accurate and early stage diagnostic, as algorithms in the screening of adrenal hyperfunction. In all dogs from the study group, the basal cortisol levels revealed a significant increasing, in comparison with normal values. In patients with hyperadrenocorticism, the liver failure was marked and defined by increases (with statistically significant) in serum transaminases and Alkaline Phosphatase activity. Also, in dogs with Cushing's syndrome, the cholesterol showed a constant and moderate increasing. In order to confirm the diagnostic, to perform a differential diagnostic (between pituitary and peripheral origin) of adrenal changes and to exclude certain diseases with similar symptoms, it was recommended and performed the ultrasound evaluation.*

## INTRODUCTION

Internal medicine of the companion animals is a vast field, which is in continuous development in veterinarians worldwide. Literature data mentions that Polyuria-Polydipsia syndrome, occurs in 80-85% of dogs with hyperadrenocorticism (Cushing's syndrome), and sometimes is really the only symptom of it, which makes clinical approach and differential diagnosis extremely important. In most cases, common causes of polyuria and polydipsia accompanying various diseases (hyperadrenocorticism, insipid or mellitus diabetes, pyometra, chronic renal failure), suspicioned as well by other different clinical signs and confirmed by laboratory tests, through specific and obvious changes. Thus, a complete biochemical screening is an efficient means in identification or exclusion of many diseases associated with Polyuria-Polydipsia syndrome (Feldman, 2005).

## MATERIALS AND METHODS

The study was performed on 24 dogs, divided in 2 groups: the control group consisting from 12 clinical healthy dogs and the second group constituted by 12 dogs with hyperadrenocorticism. The dogs from the both studied groups were of different breeds, gender or age. The existence of individual variations (breed, age, weight, gender, dietary features, state of body care and maintenance) has imposed as to the diagnostic conclusion, to take into account, the average value for each parameter (hematological or biochemical) and compare to the reference values. The results were statistically processed, obtaining the average and the standard error of the average ( $X \pm Sx$ ). For statistical signification assignment, the differences between groups were compared through Student Test.

The patients from the studied batches were evaluated according to the same investigational protocol: anamnesis, clinical examination, biochemical examination and ultrasonographic evaluation, filling for each patient from the study, a clinical record and a treatment tracking file.

Because the volume of serum that expresses represents about 45-50% of total blood collected, for biochemical evaluations in dogs, the amount of blood required was of 2-6 ml (enough for a single sample).

From the blood biochemical panel were selected some partial profiles: endocrine profile - basal cortisol; enzyme profile - serum transaminases (ALT and AST) and Alkaline Phosphatase, activity and energy profile - cholesterol, after assessing the anamnesis and specific clinical signs.

In Cushing's syndrome the adrenal impairment is accompanied by morphological and eco-structural alterations, appreciable by ultrasound method that ranks priority in terms of relevance and specificity (Codreanu et al, 2009, Wood et al, 2007).

In order to confirm the diagnosis and to exclude certain diseases with similar symptoms were performed ultrasound evaluations, using Mylab 30 and Aquila-Vet Esaote devices (with convex probes of 7.5 and 8 MHz). For these purpose adrenals ultrasound was performed using high frequency transducers (linear or convex probes of 8-18 MHz) on 12 dogs with hyperadrenocorticism.

## RESULTS

For the diagnostic algorithm optimization and for limiting the overall causal and in order to optimize the therapeutic approaches, the clinical examination data in dogs with hyperadrenocorticism, were corroborated with the results of biochemical tests and ultrasonographic evaluation.

In all patients from the studied group (n=12), initially suspected and later confirmed with hyperadrenocorticism (100%), the clinical dominant aspect was Polyuria - Polydipsia syndrome with polyphagia (50% of them). Additional to this dominant syndrome, the most frequent clinical signs and intensely expressed in patients with hyperadrenocorticism (Cushing's syndrome), were bilateral dorsal alopecia (75.0 %) and abdominal ptosis (66.6 %).

Physical examination of internal organs revealed hepatomegaly in 38.8% of dogs with hyperadrenocorticism reflected and defined by significant increasing of serum transaminases (ALT and AST) and Alkaline Phosphatase activity.

In Table 1 are presented the mean of basal cortisol level, of serum transaminases and Alkaline Phosphatase activity and the mean values of the cholesterol, from the studied group, compared to the control group mean values.

**Table 1: The average values of some biochemical parameters in studied dogs with hyperadrenocorticism (Cushing's syndrome)**

Parameters	Units of measurement	Studied group (n=12)	Control group (n=12)	Reference values
Basal cortisol	mg/dl	7.48**	4.28	0,5-6

ALT	U/l	98.1**	38.2	8-57
AST	U/l	81.8**	42.1	9-49
Alkaline Phosphatase	U/l	427.6**	87.6	11-100
Cholesterol	mg/dl	290.5*	173.2	116-254

n – number of dogs, \* p>0,05 – insignificant differences, \*\* p<0,05 - significant differences

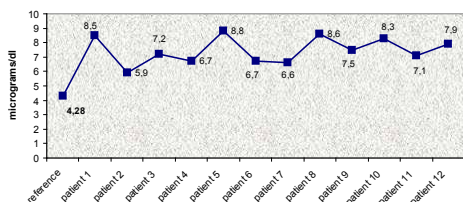
After dosing the activity of serum transaminases, ALT - 98.1 U/l (75÷134 U/l) and AST - 81.8 U/l (64÷96 U/l) were recorded significantly higher mean values, compared to reference values cited in specialized literature, denoting in studied animals, serious secondary liver damage.

The mean value of Alkaline Phosphatase activity, 427.6 U/l (375÷5784 U/l) is also significantly higher than the mean value registered in the control group (87.6 U/l).

Regarding the mean value of cholesterol (290.5 mg/l), was also higher, but not statistically significant compared to the reference value cited by the specific literature (116-254 mg/dl).

The mean value of the basal cortisol, 7.48 µg/dl (5.9÷8.8 U/l), dosed in dogs with hyperadrenocorticism (Cushing's syndrome), was significantly higher than the mean value of the control group (4.28 µg/dl), extremely suggestive in confirming this endocrine disease, in all dogs from the study group (Fig. 1).

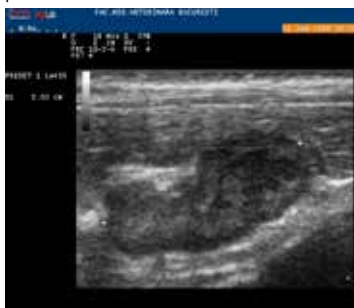
Figure 1. Basal cortisol level in dogs from control group and in dogs with hyperadrenocorticism



After corroborating the clinical signs with the elevated basal cortisol levels and serum biochemical obtained data (based on the main hepatic parameters), the main presumption of diagnosis is for the Cushing's syndrome, confirmed by the changes of echotexture and echogenicity of the adrenal glands, identified by ultrasound examination (Bourdeau et al, 2007, Marin et al, 2012).

Ultrasound reveals in case of affected adrenal glands that appears as distinct structures, flattened shape appearance lobe, located cranio-medial relative to kidney, caudal of the mesenteric and celiac artery and cranial of the renal artery – for the left gland, and for the right (lower), prior to renal vein and cranial right kidney (Codreanu et al, 2009). The sonographic evaluations of the affected patients revealed systemic changes, but generally nonspecific at the parenchymatous organs' level, with high degree of specificity in case of adrenals (Fig. 2).

Fig. 2. Left adrenal hypertrophy in a dog with pituitary hyperadrenocorticism



The left adrenal gland with obvious hypertrophic aspect, global hypoechogenicity and a noticeable weak corticomedullary demarcation (18 MHz linear probe).

In case of pituitary hyperadrenocorticism was noticed a bilateral adrenomegaly with an obvious maintained corticomedullary demarcation (maintaining the specific echogenicity differences).

In other patients, the ultrasound investigation also revealed an enlarged liver, spleen or kidney, with moderate congestive-infiltrative appearance, generally without signification. No free accumulation in hollow spaces was registered. In kidney, no corticomedullary alterations of the apparent ratio were reported; the echostructure was generally, homogeneous. The urinary bladder is relaxed because the abundant content, without parietal changes.

In case of adrenal dependent Cushing's syndrome was registered unilateral involving of the glands, with sonographic identifiable changes of volume, echotexture and/or echogenicity. These features have high degree of specificity, indicating the affection of the adrenal glands (Fig. 3), in many cases with secretory repercussions (Behrend et al, 2005).

Fig. 3. The right adrenal gland in a dog with hypercorticism



The right adrenal gland of hypertrophic aspect, with irregular shape, enhanced echogenicity and inhomogeneous echotexture (central hypoechogenicity and peripheral medium) high elevated echogenicity). Big sized adrenal tumour of macro-nodular aspect (convex 7.5 MHz probe).

The ultrasound investigation in case of adrenal dependent Cushing's syndrome reveals the presence of tumoral masses, or different inhomogeneous areas, in correlation with raised levels of the serum cortisol. In addition, the abdominal sonographic evaluation could emphasize other structural inhomogeneous areas in the parenchymal organs (liver, spleen, kidneys), as primary or secondary tumor.

This protocol of investigations: clinical coordinates, serum biochemical changes, ultrasonography in addition with basal cortisol level was configured in order to establish a facile algorithm of diagnostic in suspected hyperadrenocorticism and for achieving data regarding the main functional disturbances of the liver, in accordance and induced mainly by the cortisol in excess. This goal is accomplished and the protocol suppose less expensive investigations, which can represent a real alternative of the classical tests of serum cortisol dosing (suppression with dexamethasone or ACTH stimulation), followed by complete biochemical investigation for the major parenchymatous organs, described and recommended by the specific literature (Grossman et al, 2006, Ruckstuhl et al, 2002).

CONCLUSIONS

The main clinical signs in all suspected patients with hyper-

adrenocorticism, were represented by Polyuria-Polydipsia syndrome, bilateral dorsal alopecia, abdominal ptosis and also by hepatomegaly, reflected and defined, by statistically significant increasing of the serum transaminases (ALT and AST) and Alkaline Phosphatase activity.

The certain diagnostic of hyperadrenocorticism was based on the increased levels (with statistical significance) of the serum basal cortisol, in all dogs from the studied group.

Using ultrasound technique could be easily identified and pointed out the bilateral hypertrophy of the adrenals - in case of pituitary hyperadrenocorticism, or in on order to emphasize the character and specificity of the secreting pathological processes (tumors, cysts) at the adrenal level, in case of adrenal-dependent Cushing's syndrome.

The recommended protocol based on corroborating the main clinical coordinates, hepatic serum biochemical changes, ultrasound changes with the elevated levels of serum basal cortisol, can be considered a facile algorithm for the diagnostic in hyperadrenocorticism.

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