RESEARCH ARTICLE

Clinical and Haemato-biochemical Characteristics of Hypothyroidism in Canines

Harneet Kour*, Sushma Chhabra, Charanjit S. Randhawa

Abstract

Hypothyroidism is one of the common endocrine disorders of dogs. The present study was conducted from June 2018 to February 2020 at Small Animal OPD of the University, Ludhiana, Punjab. The hospital prevalence of hypothyroidism was found to be 0.174% (35/20102). The mean total thyroxine level (0.44 ± 0.61 µg/dL) in hypothyroid dogs was significantly ($p \leq 0.01$) lower, whereas the mean thyroid-stimulating hormone (TSH) level (6.79 ± 0.01 ng/mL) was significantly ($p \leq 0.01$) higher as compared to healthy dogs. The most common clinical characteristics associated with hypothyroidism were metabolic signs, particularly lethargy (51.43%), obesity or weight gain (80.08%), exercise intolerance (68.57%) and dermatological abnormalities including bilateral alopecia (85.71%), rat tail appearance (71.42%), hyperpigmentation (28.57%), pruritus and poor coat quality (14.28% each). The haemato-biochemical changes included elevated TLC, hypercholesterolemia, hyper-triglyceridemia, significantly higher ALP, hypocalcemia, and hypophosphatemia. These results confirmed that thyroid hormones play a significant role in maintaining the body's metabolic equilibrium and the integrity of different organs, such as the liver, kidney, and skin.

Keywords: Dogs, Hypercholesterolemia, Hypothyroidism, Thyroid-stimulating hormone, Thyroxine.

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Introduction

Hypothyroidism is the clinical condition considered one of the most common canine endocrine disorders. Thyroid hormones influence the metabolism of most of the organs in the body. The hypothyroidism results from the impaired production and secretion of thyroid hormones. It may result due to dysfunction of any part of the hypothalamic-pituitary-thyroid axis, and mostly associated with a deficiency of thyroxine (T4) and triiodothyronine (T3) hormones resulting in different cutaneous and noncutaneous clinical signs (Bhatt *et al*., 2018). Hypothyroidism may also result from atrophy of the thyroid tissue and resultant infiltration of the tissue by fat or by cancer. Depending on whether the cause is involved in thyroid gland, pituitary gland or hypothalamus, it can be classified as primary, secondary and tertiary hypothyroidism (Das *et al*., 2021). The prevalence of hypothyroidism has been reported to be 0.2-0.8% and commonly affects middle-aged and neutered dogs (Kumar and Ramesh, 2011). The clinical signs of hypothyroidism are therefore variable and nonspecific. In general, overt and subclinical hypothyroidism was associated with hypercholesterolemia (Mullur *et al*., 2014). 20 to 76% of the hypothyroid dogs are presented with complaints of weakness, lethargy or exercise intolerance (Scott-Moncrieff and Guptill-Yoran, 2000). Diagnosis of canine hypothyroidism can be challenging because several other diseases can present with similar clinical signs. This study aimed to identify clinical and haemato-biochemical characteristics of hypothyroid dogs diagnosed by reliable techniques.

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Materials and Methods

The present study was conducted on 20,108 dogs aged one year or greater presented for various health reasons from June 2018 to February 2020 to small animal OPD, Teaching Veterinary Clinical Complex, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab. Suspected cases were subjected to a comprehensive clinical and laboratory examination for the identification of underlying endocrine diseases.

The complete health record of suspected dogs, including age, breed, sex, body weight, type of diet given, nature of the illness, dermatological abnormality, any previous treatment, were recorded. Some of the dogs with dermatological problems were additionally having other clinical signs like metabolic disorders, reproductive disorders, etc., that were suggestive of hypothyroidism.

Routine hematological and biochemical estimations along with thyroid function test were recommended. The animal was properly restrained, and 2 mL of whole blood was collected aseptically from the cephalic or saphenous vein in a vial coated K_3EDTA for determination of hemoglobin (Hb), total leukocyte count (TLC), and differential leukocytes count (DLC). For estimation of biochemical parameters, 8 mL of blood was collected without anticoagulant for serum separation. Collected serum samples were used for estimation of various biochemical parameters using a fully automatic Vitros DT 350 Chemistry system (Ortho Clinical Diagnostics, Johnson & Johnson Company). Thyroid-stimulating hormone (TSH) and total thyroxine (T4) estimation were done using canine-specific sandwich ELISA kit of Bioassay Technology Laboratory and Sino Gene Clon Biotech Company limited according to the guidelines provided by them. Serum samples were used for estimation of TSH and T4, and kits were stored at 4°C before use. In addition, skin scrapings and blood smears were examined for the presence of ectoparasites and hemiparasites. The data generated were mean ± standard errors and compared between healthy and diseased groups by the 't' test for statistical significance at $p < 0.05$.

Results and Discussion

Hormonal Status of Hypothyroid Dogs

On the basis of low levels of T4 and higher levels of TSH, a total of 35 dogs were diagnosed with hypothyroidism. In the present study, the hospital prevalence of hypothyroidism was found to be 0.174 (35/20102). In the hypothyroid dogs, the mean total thyroxine level (0.44 ± 0.61 vs. 2.17 ± 0.26 µg/dL) was significantly ($p \leq 0.01$) lower, and mean TSH levels (6.79 ± 0.01 vs. 0.95 ± 0.04 ng/mL) was significantly ($p \leq 0.01$) higher as compared to that of healthy dogs (Table 1). These findings were in agreement with Jagpreet *et al.* (2006), who stated that the diagnosis of hypothyroidism was achieved by demonstration of low T4 and elevated TSH concentrations. Chakraborty (2007) and Gulzar *et al.* (2014) opined that estimation of T4 is a specific diagnostic tool for identifying hypothyroidism in dogs. Suraniti *et al.* (2008) reported that the measurement of canine-thyrotropin had an excellent specificity, and TSH could be a valuable tool in confirming canine hypothyroidism.

Clinical Manifestations of Hypothyroid Dogs

Clinical signs of canine hypothyroidism were extremely variable and included both systemic and dermatological signs (Figs. 1-3). The common clinical manifestations observed among 35 hypothyroid dogs were polydipsia/polyuria (88.57%), heat-seeking (88.57%), bilateral alopecia (85.71%), obesity (80.08%), rat tail appearance (71.42%), exercise intolerance (68.57%), lethargy (51.43%), anemia (37.14%), dyspnoea (34.28%), hyperpigmentation (28.57%), pale mucous membrane (28.57%), secondary skin disorders (22.8%), pruritus and dry and lusterless coat (14.28% each), cyanosis and myxedema (8.57%) and nervous signs (5.71%). These findings were in agreement with Kumar *et al.* (2007). The clinical signs of the disease varied greatly because of the myriad of systems the thyroid hormone impacted. Bhatt *et al.* (2018) reported that thyroid hormones were required to initiate anagen hair follicles, cornification process regulation, and sebaceous gland secretion. In hypothyroid animals, most hair follicles were retained in the telogen phase, causing the hair coat to be dry, dull, and brittle. Hair loss was noted in areas of increased wear and usually included the ventral thorax and neck, ventral abdomen and tail. Loss of primary hair was

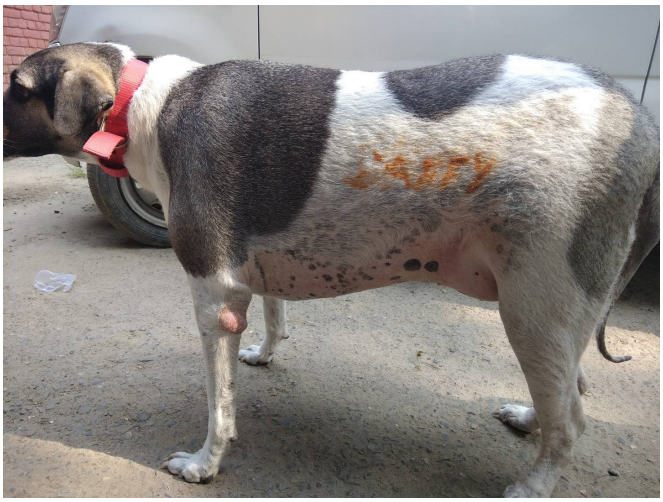

Fig. 1: Obese hypothyroid dog

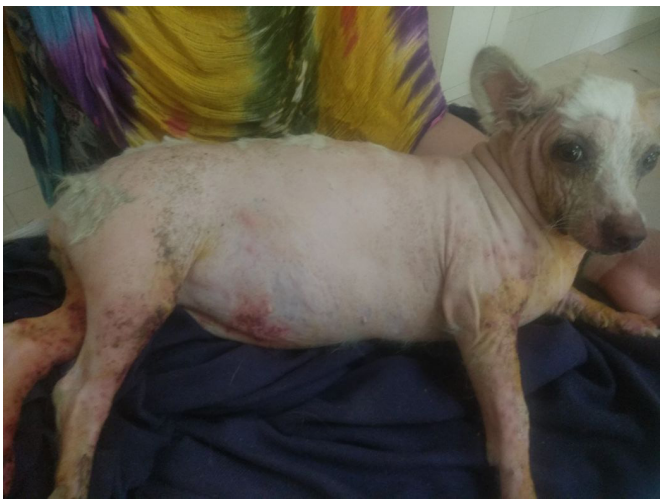

Fig. 2: Alopecia in hypothyroid dog

Table 1: Status of thyroid hormones in hypothyroid dogs (Mean ± SE)

Hormones	*Healthy dogs (n=10)*	*Hypothyroid dogs (n=35)*	*P value*
T4 (ug/dL)	2.17 ± 0.26 (1.21-3.65)	0.44 ± 0.61** (0.19-1.01)	0.00
TSH (ng/mL)	0.95 ± 0.04 (0.09-1.08)	6.79 ± 0.01** (2.67-10.54)	0.00

Figures in parentheses indicate range. **Significant at 1% level ($p < 0.01$).

most common with retention of guard hairs, resulting in a short and fine hair coat. In the hypothyroid state, there was decreased T-cell function and humoral immunity, making skin more susceptible to infection and recurrent dermatitis (Mayr, 2007). Kumar *et al.* (2007) reported that 8.85% of symptoms could arise from the peripheral nervous system and cranial nerves and stated that in hypothyroidism, nerves do not conduct electrical impulses normally. This could account for general weakness, exercise intolerance, lethargy and listlessness observed in hypothyroidism. Seizures. Myxedema (cutaneous mucinosis), a rare dermatological manifestation of hypothyroidism, might be attributed to an accumulation of excessive amounts of mucopolysaccharides and protein in the dermis that might also occur in facial nerves resulting in facial paralysis (Mooney, 2011). Pruritus, could occur with concurrent infections, whereas impaired neutrophil and lymphocyte function result in pyoderma and sebhorrhoea. Kumar *et al.* (2007) who documented similar signs related to decreased metabolic rate. The presence of lethargy was frequently overlooked, as owners might notice abnormality only after thyroid hormone supplementation resulting in increased activity and alertness, hence indicating neuropathy or myopathy (Mayr, 2007). The present research findings also corroborated with Rossmeisl *et al.* (2009), who documented that chronic canine hypothyroidism resulted in substantial but subclinical phenotypic myopathic changes indicative of altered muscle energy metabolism and depletion of skeletal muscle carnitine.

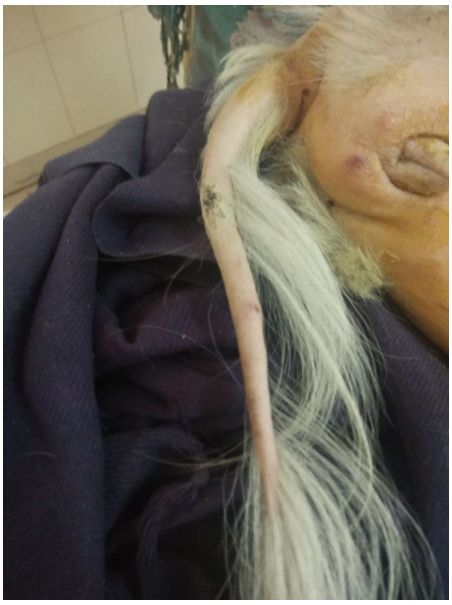

Fig. 3: Rat tail in hypothyroid dog

Physiological Parameters of Hypothyroid Dogs

Mean values of various physiological parameters like rectal temperature, respiration rate, and heart rate are presented in Table 2. Significantly lower ($p < 0.05$) heart rate recorded in the present study was in agreement with Gaalova *et al.* (2008) who recorded low heart rate and bradyarrhythmias and bradycardia and weakness with hypothyroidism in dogs.

Hematological Alterations

The hematological findings of the hypothyroid dogs revealed normocytic, normochromic, non-regenerative anemia in 14 dogs (40%). However, significantly low ($p \leq 0.05$) mean levels of PCV along with a significantly ($p \leq 0.01$) higher TLC were recorded among hypothyroid dogs (Table 3). The mean TLC value of hypothyroid dogs (13432.15 ± 121/ul),

Table 2: Vital body parameters of hypothyroid dogs (Mean ± SE)

Clinical parameters	*Healthy dogs (n=10)*	*Hypothyroid dogs (n=35)*	*P Value*
Respiration rate (per min)	27.6 ± 0.31 (18-35)	33.18 ± 1.3 (14-79)	0.27
Rectal temperature (°F)	101.4 ± 0 .98 (99.8-102.8)	101.9 ± 0 .12 (100-104)	0.15
Heart rate (beats per min)	84.9 ± 2.4 (74-98)	81.15 ± 1.6* (46-90)	0.021
Mucus membrane	Normal	Pale	--

Figures in parentheses depict range.

Table 3: Haematological profile of dogs with hypothyroidism (Mean ± SE)

Parameter	*Healthy dogs (n=10)*	*Hypothyroid dogs (n=35)*	*P Value*
Haemoglobin (g/dL)	12.94 ± 0.33 (11-14.7)	11.63 ± 0.24 (6.8-13.8)	0.13
TLC (count/µl)	11360.8 ± 154 (10466-13100)	13432.15 ± 121** (9300-21543)	0.01
TEC (x10^6/µl)	5.67 ± 0.20 (4.78-6.67)	5.61 ± 0.11 (4.5-7.44)	0.47
PCV (%)	38.08 ± 0.63 (34.9-41)	36.87 ± 0.76* (31.2-37.8)	0.03
Platelets (x 10^3/µl)	178.6 ± 11.01 (119-230)	177.87 ± 23.94 (98-255)	0.067
Neutrophils (%)	81.6 ± 2.20 (70-92)	83.76 ± 2.13 (67-94)	0.23
Lymphocytes (%)	13.2 ± 2.33 (2-26)	12.23 ± 0.85 (2-22)	0.75
Monocytes (%)	0.8 ± 0.44 (0-4)	0.6 ± 0.05 (0-6)	0.19
Eosinophils(%)	1.2 ± 0.61 (0-6)	1.48 ± 0.34 (0-8)	0.48

Figures in parentheses indicate range. *Significant at 5% level ($p \leq 0.05$), **Significant at 1% level ($p \leq 0.01$).

Table 4: Status of various biochemical parameters in hypothyroid dogs (Mean ± SE)

Clinical markers	*Parameters*	*Healthy dogs (n=10)*	*Hypothyroid dogs (n=35)*	*P Value*
Hepatic profile	Total protein (g/dL)	5.92 ± 0.10 (5.1 - 6.2)	5.6 ± 0.11* (2.2 - 8.1)	0.039
	Albumin (g/dL)	3.88 ± 0.09 (2.9 - 4.2)	3.07 ± 0.06 (2.7 - 4.3)	0.379
	AST (IU/L)	49.5 ± 4.47 (33 - 76)	50.4 ± 1.49 (39 - 65)	0.341
	ALT (IU/L)	66.9 ± 4.56 (47- 89)	70.9 ± 7.05 (38 - 98)	0.07
	ALP (IU/L)	96.7 ± 2.88 (80 - 108)	192.24 ± 0.88** (93-370)	0.011
Renal marker	BUN (mg/dL)	9.1 ± 0.64 (6 - 12)	9.79 ± 0.42 (7.0 - 11.5)	0.21
	Creatinine (mg/dL)	0.63 ± 0.10 (0.3 - 1.3)	0.74 ± 0.2 (0.3 - 1.7)	0.32
Obesity markers	Triglycerides (mg/dL)	89.2 ± 5.18 (56 - 110)	128.24 ± 7.12* (67 - 159)	0.03
	Total cholesterol (mg/dL)	167.5 ± 5.7 (145 - 198)	298.3 ± 8.77** (178 - 478)	0.001
Glucose marker	Glucose (mg/dL)	96.3 ± 2.48 (85 - 108)	149.3 ± 16.68** (88 - 179)	0.011
Minerals	Calcium (mg/dL)	10.53 ± 0.15 (9.8 - 11)	9.97 ± 0.26* (9.2 - 12.8)	0.032
	Phosphorus (mg/dL)	5.25 ± 0.19 (4.00 - 6.00)	4.78 ± 0.26* (3.6 - 6.2)	0.02

Figures in parentheses indicate range. *Significant at 5% level ($p \leq 0.05$), **Significant at 1% level ($p \leq 0.01$).

was significantly ($p \leq 0.01$) higher than healthy dogs (11360.8 ± 154 /ul). The mean PCV (36.87 ± 0.76%) in hypothyroid dogs was significantly lower ($p < 0.05$) as compared to healthy dogs (38.08 ± 0.63%). The observations recorded in the present investigation were in accordance with the reports by Andronic *et al.* (2008), Rossmeisl *et al.* (2009), and Dorgalaleh *et al.* (2013) in hypothyroid dogs. It was reported that thyroid hormones enhanced erythropoiesis through the hyperproliferation of immature erythroid progenitors and increased secretion of erythropoietin (EPO) by inducing erythropoietin gene expression. In the hypothyroid state, decreased T-cell function and humoral immunity causing secondary bacterial/fungal or parasitic infection, resulting in increased total leukocyte count.

Blood Biochemical Alterations:

The mean values of ALP, triglyceride, cholesterol, and glucose concentration were significantly higher ($p \leq 0.05$), and the mean values of calcium and phosphorus were significantly lower ($p \leq 0.05$) in dogs with hypothyroidism as compared to normal dogs (Table 4). The findings of the present study were in accordance with Andronic *et al.* (2008) who reported elevated levels of liver enzymes in hypothyroidism probably due to degenerative hepatopathy and myopathy caused by fat infiltration and hyperlipidemia that could lead to atherosclerosis in hypothyroidism. Rossmeisl *et al.* (2009) and Mazaki *et al.* (2015) documented that hypercholesterolemia occurred in 75% of hypothyroid dogs, whereas hypertriglyceridemia occurred in 88% of the dogs. Decreased thyroid function was accompanied by reduced activity of HMG-CoA reductase (3-hydroxy3methylglutaryl-coenzyme A). Hence, the total cholesterol and triglyceride levels were increased. This could be due to the decreased LDL-receptors activity and IDL (Intermediate density lipoproteins) causing decreased clearance of triglycerides-rich lipoproteins. Therefore, overt hypothyroid patients might also present with elevated triglyceride levels associated with increased VLDL levels (very-low-density lipoprotein cholesterol) (Rizos *et al.,* 2011). Blood glucose levels in the present study were increased in hypothyroid dogs; the results were in accordance with Taguchi *et al.* (2010), who found that thyroid hormones exerted profound effects in the regulation of glucose homeostasis, including modification of circulating insulin levels and counter-regulatory hormones, intestinal absorption, hepatic production and peripheral tissues (fat and muscle) uptake of glucose. In another study, Johnstone *et al.* (2014) reported the aetiology of insulin resistance diabetes mellitus (IR) in naturally occurring canine hypothyroidism. Excess secretion of growth hormone (GH) by trans-differentiated pituitary cells might have contributed to insulin resistance in some hypothyroid dogs. Yousif *et al.* (2012) noticed hypocalcemia in groups of induced hypothyroidism.

Hypothyroidism also influenced membrane transport and electrolyte metabolism and alterations in mineral metabolism, which frequently caused calcium nephropathy (Suraniti *et al*., 2008).

Conclusion

In hypothyroidism, the most common clinical signs recorded were lethargy, obesity, exercise intolerance, bilateral alopecia, and rat tail appearance. The biochemical changes included a significant reduction of T4, increased TSH, hypercholesterolemia, hyper-triglyceridemia, elevated ALP, hypocalcemia, and hypophosphatemia. The combination of dermatological and metabolic abnormalities should prompt the identification of hypothyroidism. These results confirmed that thyroid hormones play a significant role in maintaining the body's metabolic equilibrium and the integrity of different organs, such as the liver, kidney, and skin.

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