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1 Pawing for answers: The tail of canine hypothyroidism

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Abstract
In the present study, total 3952 dogs were registered at the Veterinary Clinical Complex, Anand during the nine month period. Of these, 567 cases had reoccurring dermatological disorders in dogs, prevalence of canine dermatoses was found to be 14.34 percent. The incidence of endocrine dermatoses was 7.83 percent of dermatology case loads of the Veterinary Clinical Complex, Anand in the study period. The most common endocrine dermatoses were that of hypothyroid and dermatologic signs observed in hypothyroidism included symmetrical alopecia, thin/sparse coat, dry, brittle hair, rat tail, seborrhea and pyoderma. Diagnosis was made based on history, clinical signs and by CLIA and treatment of dogs suffering from hypothyroid dermatoses with levothyroxine @0.02 mg/kg BW resulted in regrowth of hair, reversal of dermatologic and physical signs.

Keywords: Hypothyroidism, Levo-thyroxine, Thyroid hormones, CLIA, Canine dermatology, Canine endocrinology

Introduction
Canine dermatology is a significant field of medicine for a variety of reasons, as one of the most aesthetic joys of dog ownership is the sight of a shiny, healthy-looking, colorful coat of fur. Canine dermatoses range from acute, self-limiting issues to chronic or enduring issues requiring lifelong therapy. The skin, hair, and subcutaneous tissue of a newborn puppy represent 24.00% of its body weight; by the time of maturity, these structures represent approximately 12.00% of body weight (Scott *et al.*, 1995) [22]. In addition to the unappealing appearance of the affected animal and the chronic nature of the skin ailment, the skin's defensive function also weakens (Feijo *et al*., 1998) [6]. Therefore, dermatological afflictions need considerable attention with regard to their diagnosis and treatment. Dermatological disorders are the most common conditions seen in small animal clinics, and it has been estimated that between 20.00% and 75.00% of small animals seen in the average practice have skin problems as the primary or secondary owner complaints (Scott and Paradis, 1990) [21].
Animals are incredibly complex multicellular organisms, requiring many simple to very sophisticated control mechanisms to maintain a state of physiologic and biochemical equilibrium. Despite its complexity and its functionality, which is incredibly effective, the control of its basic functions is performed by only two systems: the nervous system and the endocrine system, which acts through the synthesis and release of chemical messengers and are responsible for several functions of the organism in a slower yet durable way (Feldman and Nelson, 2004) [7]. In dogs, dermatological lesions are a common manifestation of endocrine disorders. Three hormones - thyroxine, cortisol, and estrogen have a significant impact on hair development. As a result, one of the primary causes of adult onset symmetrical alopecia in dogs worldwide is endocrine dermatoses, which are frequently triggered by endocrine disorders such as hyperadrenocorticism (HAC), hypothyroidism, and hyperestrogenism due to testicular sertoli cell tumours (Frank, 2006) [10].
Dermatology and endocrinology are veterinary specialties on the rise today. Canine endocrine dermatopathies account for 8.60% of dermatological appointments, frequently presenting classic signs of non-pruritic bilaterally symmetrical alopecia that develops chronically (Scott& Paradis, 1990; Scott *et al.*, 2001) [21, 23].

Symmetrical alopecia in dogs is more than a cosmetic problem in many ways. It may be an outward sign of an underlying condition that could have grave repercussions. Lack of hair growth in previously clipped areas could be a sign of an underlying endocrinopathy.

Hypothyroidism is the most typical canine endocrinopathy. It can be primary or secondary, and its aetiology might be acquired or congenital (Castillo, 2011) [1]. Thyroid hormones perform several functions involving multiple tissues and organ systems. Thyroid hormone deficiency can thus cause a variety of clinical symptoms and influence numerous body systems, including the skin, cardiovascular, neurological, reproductive, and other endocrine systems (Dixon, 2001) [4]. The most prevalent endocrinopathy is characterized by alopecia in areas of wear, seborrhea, and recurring infections. Thin, dry, and dull hair coats, symmetric alopecia, lack of hair growth after trimming, weight gain or obesity, fatigue, weakness, and hyperpigmentation are common clinical manifestations linked with hypothyroidism. The pressure points (elbows and hips), the entire length of the tail ("rat tail"), around the neck (from the collar), and the bridge of the nose are the most prevalent areas of alopecia. There may be a preferential loss of guard hairs, exposing the very fine undercoat hairs and creating the impression of a "puppy coat". The diagnosis of hypothyroidism is undeniably problematic because none of the individual clinical indicators are pathognomonic for the disease and are frequently coupled with other diseases. Hypothyroidism is diagnosed using a combination of symptoms, history, physical examination, routine clinicopathological findings, and specific thyroid function testing (Credille *et al*., 2001) [2].

Materials and Methods

In the present study at the veterinary clinical complex, 3952 dogs were presented during the nine month period from November, 2022 to July, 2023 for the treatment of various ailments. A total of 567 cases of dogs, irrespective of age, breed, or sex, showed signs of recurring dermatoses. Suspected cases were subjected to a comprehensive clinical, dermatological, and laboratory examination for the identification of underlying endocrine diseases. On the basis of history and clinical symptoms, dogs were categorized into various endocrine disorders irrespective of age, sex, and gender. Cases presented with a dry, brittle hair coat, seborrhea and symmetric alopecia, lack of hair growth after trimming, heat seeking, anorexia and weight gain or obesity, lethargy and exercise intolerance, weakness, and a rat-tail appearance were selected and screened for hypothyroid dermatoses. All the dogs presented with clinical signs of endocrine dermatoses were examined, and samples were taken for further hormonal assay. Eighteen dogs with confirmatory endocrine dermatoses were subjected to therapeutic management for hypothyroidism with levothyroxine and supportive medications. Clinical signs and laboratory parameters were studied in the clinical cases. Hemato-biochemical and hormone values of the control group dogs were estimated for the establishment of reference normal values for the study. Serum samples of suspected cases showing clinical signs of hypothyroidism were analyzed on the same day by CLIA. Serum samples of Total T4 (TT4), free T4 (fT4) and Thyroid stimulating hormone (TSH) were collected on day 0 (day of presentation) and on day 45 for diagnosis and therapeutic monitoring of hypothyroidism, respectively. Cases with hypothyroid dermatoses were managed with oral Levothyroxine therapy at the dose rate of 0.02 mg/kg b.i.d P.O as suggested by Scott-Moncrieff (2007) [25] and Ferguson (2007) [9]. The dog owners were instructed to visit at 6 weeks interval after initiation of therapy. The therapeutic efficacy was assessed based on clinical response and by measurement of serum fT4, TT4 and TSH estimation (Dixon *et al*., 2001) [4]. At about 45 days after beginning of treatment, blood sample was collected six hours after post pill administration of Levothyroxine and serum total T4, free T4 and TSH were estimated. The dose of Levothyroxine was re-evaluated based on clinical and hormonal response. The hematology and biochemical findings were estimated prior to therapy and post treatment of hypothyroid dogs. Secondary Demodicosis was treated with injectable ivermectin @200µg/kg body weight weekly. Medication was continued till two consequent skin scrapings proved negative for Demodex mites at an interval of seven days. *Malassezia* dermatitis was treated with oral ketoconazole @10mg/kg body weight per day upto resolution, liver supportive orally along with ketoconazole shampoo weekly. Dogs were treated for pyoderma with various antibiotics depending upon the severity of condition and ABST results. The data obtained through haemato-biochemical and hormonal examinations in the research work were statistically analyzed and clinical variants were subjected to independent t-test and paired t-test by employing SPSS software 21.0. The p values >0.05 were considered as non-significant.

Fig 1: Collection of skin scraping from affected hypothyroid dog

Fig 2: Trichography/hair plucking from affected hypothyroid dog

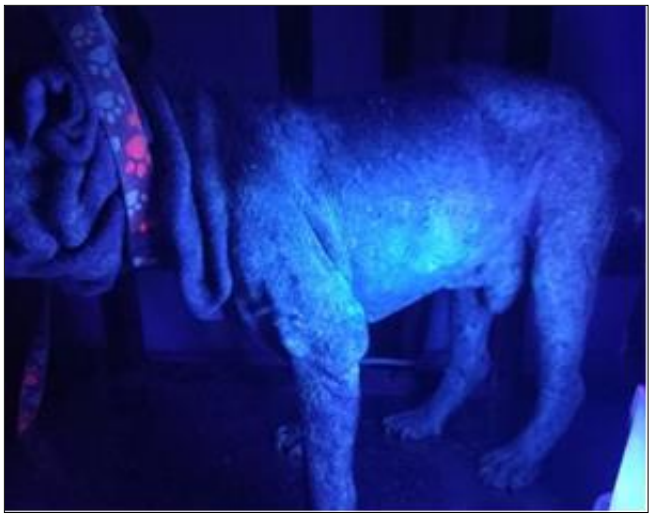


Fig 3: Wood's Lamp examination of ear and skin coat in affected dog

Results and Discussions

In the present nine-month period under study (November 2022 to July 2023), a total of 3952 dogs were registered at the Veterinary Clinical Complex, Anand, with various ailments. Out of these, 741 dogs were suspected of various skin disorders based on history and clinical signs, which accounts for 18.75% of the total cases admitted to the clinic. Skin disorder is one of the most commonly encountered problems in pet animals as dogs are susceptible to various skin problems be it parasitic, fungal, bacterial skin disease or allergies of various origin. These findings simulate with the findings of Scott and Paradis (1990) [21], who reported that dermatological problems accounted for 18.80% of all dogs examined at the Small Animal Clinic, University of Montreal, Saint-Hyacinthe, over a one-year period. Canine dermatoses can have diverse underlying causes, 567 recurring dermatoses dogs were subjected to various etiologies based on their clinical conditions and 58 dogs (10.23%) had hormonal imbalances and out of 58 dogs suspected of hormonal imbalances, 32 were suspected and screened for hypothyroidism based on history and clinical signs and were subjected to thyroid hormone measurements. Eighteen dogs were confirmed for hypothyroidism and were subjected to further treatment. In the present study the prevalence of hypothyroidism was found to be 3.17 percent (18/567) among total recurring dermatoses cases and the hospital prevalence was found to be 0.46% (18/3952). This finding was in close agreement with the earlier reports of Dixon (2001) [4] who estimated 0.20% to 0.64% prevalence of hypothyroidism; Srikala and Kumar (2014) [26] who reported overall prevalence of about 0.46%; Kour *et al.* (2020) [14] who found the hospital prevalence of hypothyroidism to be 0.174% and O'Neill *et al.* (2022) [18] yielding an annual prevalence of 0.23%.

Table 1: Overall prevalence of canine hypothyroidism in the hospital population of dogs

Total number of dogs screened	Recurring dermatoses	Number of dogs suspected for hypothyroidism	Number of dogs positive for hypothyroidism	Percentage (%) of hypothyroidism among recurring dermatoses (n=567)	Percentage (%) of hypothyroidism in hospital population (n=3952)
3952	567	32	18	3.17	0.46

The highest prevalence percentage of hypothyroidism was recorded in dogs aged between 6 to 9 years (n=9, 50.00%) followed by 3 to 6 years (n=5, 27.78%) and > 9 years (n=3, 16.67%). Breed wise prevalence of hypothyroidism and was found to be higher in Labrador retriever (n=6, 33.33%), Nondescript dogs (n=5, 27.78%), Beagle and German shepherd (n=2 each, 11.11%), and each in Pointer, Shih Tzu and Pomeranian (n=1, 5.56%). The study was in accordance with Dixon *et al.* (1999) [3] and Kour *et al.* (2020) [14] who also reported that Labrador retrievers were highly predisposed

to hypothyroidism. Out of 18 dogs with hypothyroidism, 11 were male (61.11%) and 7 were female (38.89%). In the present study, 32 dogs were suspected for hypothyroidism based upon the history and clinical signs of which, 18 were confirmed by measurement of free T4, total T4 and TSH by Chemiluminescent immunoassay (CLIA). Clinical examination of 18 dogs with hypothyroidism revealed dermatological manifestations such as alopecia (generalized or localized) at neck, ventral thorax, lateral abdomen (n=16, 88.89%), thinning of hair and dry, brittle haircoat (n=12, 66.67%), seborrhea (n=11, 61.11%), failure of hair regrowth (n=10, 55.56%), hyper pigmentation (n=9 each, 50.00%), erythema (n=8, 44.44%), rat tail appearance (n=7, 38.89%), pruritus (n=6, 33.33%), hyperkeratosis (n=6, 33.33%), otitis (n=4, 22.22%) which was also observed by Greco *et al.* (1998), while myxedema was recorded in one (5.56%) hypothyroid dog which was also observed by Doliger (1995) [5]. Similar dermatological lesions were also observed by Muller *et al.* (2001) [17]; Panciera (2001) [20]; Gulzar *et al.* (2014) [12]; Srikala and Kumar (2014) [26] and Jaiswal *et al.* (2018) [13]. Alopecia was due to deficiency of thyroid hormones which were required for initiation of anagen phase of hair growth, leading to persistence of telogen due to which hairs were easily epilated. Abnormal keratinization in hypothyroid dogs resulting in hyperkeratosis and changes in sebum fatty acid content could be the primary cause of seborrhea. As the hair retains in telogen phase for long period, it resulted in failure of hair regrowth as observed in 55.56% of the dogs in the present study. Pyoderma (n=9, 50.00%), mixed bacterial and fungal infection (n=3, 16.67%), and generalized demodicosis (n=5, 27.78%) were recorded as secondary infections in hypothyroid dogs. These results were in accordance with Ferguson *et al.* (1993) [8]; Panciera (1994) [19]; Greco (1998) [11]; and Dixon (1999) [3] who observed demodicosis, *Malassezia* infections, and associated pruritus in dogs with hypothyroidism. Thyroid gland plays a critical role in regulating the body immune system, and hence, when it is depressed or compromised, the body becomes increasingly vulnerable to the assault of the pathogens, as is seen in *Malassezia* dermatitis and recurrent bacterial infections of the skin. Metabolic abnormalities recorded were lethargy (n=12/18, 66.67%) weight gain and exercise intolerance (n=10, 55.56%) and heat seeking or cold intolerance (n=5, 27.78%).

Table 2: Dermatological manifestations observed in clinical cases of canine hypothyroidism (n=18)

Sr. No.	Dermatological signs	No. of dogs affected	Percentage (%)
1.	Symmetrical alopecia	16	88.89
2.	Thinning of hair	12	66.67
3.	Dry and brittle Haircoat	12	66.67
4.	Seborrhea	11	61.11
5.	Failure of hair regrowth	10	55.56
6.	Hyper pigmentation	9	50
7.	Erythema	8	44.44
8.	Rat tail appearance	7	38.89
9.	Hyperkeratosis	6	33.33
10.	Pruritus	6	33.33
11.	Otitis externa	4	22.22
12.	Myxedema	1	5.56

In the present study, the dogs with clinical signs suggestive of hypothyroidism (n=32) were screened for measurement of thyroid hormones by Chemiluminescent immunoassay (CLIA) and their haemato-biochemical values. Total T4, free T4 and TSH estimations were carried out to confirm hypothyroidism from 32 dogs. The lowered levels of total T4 and free T4 concentration by CLIA in the present study were regarded as standard. It were recorded in 32 dogs, out of which, 18 dogs had total T4 and free T4 concentration below the reference range (i.e. less than 1.5 µg/dl for total T4 and less than 0.5 ng/dL for free T4). In the present study, mean total T4 concentration of dogs with hypothyroidism (1.03±0.07µg/dl) were highly significantly lower (p<0.01) as compared to healthy dogs (2.25±0.14µg/dl). Similarly, the mean serum free T4 (ng/dL) concentrations of dogs with hypothyroidism (0.35±0.03 ng/dL) were also highly significantly lowered (p<0.01) as compared to healthy dogs (0.83±0.06 ng/dl). There was no significant difference observed in the serum TSH concentrations between healthy (0.04±0.01) and in dogs with hypothyroidism (0.07±0.03 µIU/mL) by CLIA in the present study. Due to Negative feedback effect of TT4 on the pituitary gland, measurement of canine TSH concentration isn't an accurate indicator of thyroid dysfunction. According to Mooney (2003) [16], the diagnosis of canine hypothyroidism can be made with ease if there is evidence of low circulating total thyroxine (TT4) and high thyroid stimulating hormone (cTSH) concentrations. But occasionally, this combination does not occur, necessitating the use of additional diagnostic procedures such as free T4. Scott and Moncrieff *et al.* (2002) [24] opined that measurement of canine TSH concentration was less sensitive in dogs because of the failure of the assay to detect all isoforms of circulating TSH.

The mean RBC (× 106 /µl), hemoglobin (g/dl) and packed cell volume (%) in dogs with hypothyroidism was highly significantly lowered (p<0.01), 5.16±0.19, 11.00±0.57 and 32.01±1.32, respectively as compared to healthy dogs (7.17±0.23106 /µl, 15.75±0.66 g/dl and 47.15±1.79%), respectively. MCV (fl) in hypothyroid dogs (61.83±1.21) was significantly decreased (p<0.05) as compared to healthy dogs (65.67±1.05). The total leukocyte count (103 /µl) and neutrophils were highly significantly increased (p<0.01) in dogs associated with hypothyroidism as compared to healthy dogs. There was significant increase (p<0.05) in the monocyte count of dogs with hypothyroidism (1.15±0.21) in compare to healthy dogs (0.56±0.09).

The mean serum cholesterol (mg/dl) value in the dogs with hypothyroidism (286.17±10.03mg/dl) was highly significantly increased (p<0.01) than healthy control (162.83±11.39mg/dl) and the mean serum BUN (mg/dl) value in the dogs with hypothyroidism (25.12±1.48mg/dl) was also highly significantly increased (p<0.01) than healthy control (19.11±1.43mg/dl). As thyroid hormone was required for the synthesis and degradation of cholesterol its deficiency could result in accumulation of lipids which may also predispose to atherosclerosis. In the present study the mean Aspartate aminotransferase (IU/L) values in dogs with hypothyroidism are significantly increased (p<0.05) as compared to healthy dogs. Significant increase (p<0.05) was observed in the values of creatinine (mg/dL), 0.53±0.09 in healthy dogs as compared to 0.83±0.07 in hypothyroid dogs.

Dogs with hypothyroidism were treated with oral administration of Levothyroxine sodium @ 20µg/kg.b.wt once daily. In majority of dogs, a starting dose of 20µg/kg.b.wt was sufficient to control both clinical and hormonal aspects of hypothyroidism (Le Traon *et al*. (2009) [15]. Therapeutic success was judged first on clinical response corroborated with the measurement of thyroid hormones and hematobiochemical changes. It was evident from the present study that the total T4 values highly significantly increased (p<0.01), 2.26±0.11 µg/dL on day 45 post therapy, as compared to 1.03±0.07 µg/dL on day 0. Similarly highly significant increase (p<0.01) for free T4, 0.88±0.06 ng/dL was seen on day 45 post therapy, as compared to 0.35±0.03 pg/dL on day 0. There was no significant change remarked in TSH concentrations by CLIA on day 45 and day 0 of treatment.

All the hypothyroid dogs showed marked clinical improvement with alleviation of clinical signs from two weeks after initiation of thyroid supplementation. Resolution of dermatological signs started after 4 weeks of initiation of therapy and it took 8 weeks for all the dogs to become normal.

Table 3: Total T4, free T4 and TSH estimation in dogs with hypothyroidism by CLIA on day 0 and day 45 (Mean ± SE)

Sr. No.	Name of the hormone estimated	Healthy dogs (n=12)	Dogs with hypothyroidism on day 0 (n=18)	Dogs with hypothyroidism on day 45 (n=18)	"p" value
1.	Total T4 (µg/dL)	2.25±0.14	1.03±0.07	2.26±0.11**	**0.001**
2.	fT4 (ng/dL)	0.83±0.06	0.35±0.03	0.88±0.06**	**0.001**
3.	TSH (µIU/mL)	0.04±0.01	0.07±0.03	0.03±0.01	0.184

Post therapy on day 45, highly significant (p<0.01) decrease was observed in WBC (10.26±0.65 × 103 /µl), Monocyte (0.46±0.08 ×103 /µl), and Neutrophils (8.18±0.51 ×103 /µl) and highly significant increase (p<0.01) was observed in values of RBC (7.10±0.14 × 106 /µl),; Hb (15.45±0.32 g/dl), HCT (45.79±0.96%).

Table 4: Haematological alterations in dogs with hypothyroidism on day 0 and day 45 (Mean ± SE)

Sr. No.	Parameters	Healthy dogs (n=12)	Dogs with hypothyroidism on day 0 (n=18)	Dogs with hypothyroidism on day 45 (n=18)	"p" value
1.	WBC (× 103 /µl)	10.58±0.44	22.26±2.22	10.26±0.65**	**0.001**
2.	Lymphocyte (×103 /µl)	1.60±0.27	2.33±0.64	1.60±0.32	0.326
3.	Monocyte (×103 / µl)	0.56±0.09	1.15±0.21	0.46±0.08**	**0.010**
4.	Neutrophils (×103 / µl)	8.38±0.38	18.09±2.11	8.18±0.51**	**0.001**
5.	Eosinophils (×103 / µl)	0.07±0.04	0.28±0.18	0.02±0.01	0.172
6.	Basophils (×103/µl)	0.02±0.01	0.38±0.35	0.01±0.01	0.312
7.	RBC (× 106 /µl)	7.17±0.23	5.16±0.19	7.10±0.14**	**0.001**
8.	Hb (g/dl)	15.75±0.66	11.00±0.57	15.45±0.32**	**0.001**
9.	HCT (%)	47.15±1.79	32.01±1.32	45.79±0.96**	**0.001**
10.	MCV (fl)	65.67±1.05	61.83±1.21	63.94±0.78	0.163
11.	MCH (pg)	21.69±0.54	21.14±0.67	21.54±0.37	0.632
12.	MCHC (g/dL)	33.36±0.50	34.18±0.78	33.66±0.36	0.571
13.	Platelets count (×103 /µl)	300.75±9.48	278.83±32.30	308.06±14.42	0.430

Post therapy on day 45, highly significant (p<0.01) decrease was observed in values of ALT (27.48±2.93 IU/L), AST (29.14±3.05 IU/L); BUN (23.60±1.46 mg/dL), and Cholesterol (173.17±8.88 mg/dL). The significant variation of laboratory values towards normalcy reflects overall response to Levothyroxine supplementation.

Table 5: Serum biochemical alterations in dogs with hypothyroidism on day 0 and day 45 (Mean ± SE)

Sr. No.	Parameters	Healthy dogs (n=12)	Dogs with hypothyroidism on day 0 (n=18)	Dogs with hypothyroidism on day 45 (n=18)	"p" value
1.	ALT (IU/L)	43.67±4.47	53.94±5.78	27.48±2.93**	**0.001**
2.	AST (IU/L)	33.00±3.95	57.22±7.82	29.14±3.05*	**0.002**
3.	Total Protein (gm/dL)	6.07±0.19	6.38±0.17	5.35±0.24**	**0.001**
4.	Albumin (gm/dL)	2.82±0.13	2.76±0.12	2.37±0.74**	**0.001**
5.	Globulin (gm/dL)	3.25±0.10	3.60±0.16	2.98±0.27*	**0.017**
6.	Creatinine (mg/dL)	0.53±0.09	0.83±0.07	0.69±0.07*	**0.039**
7.	BUN (mg/dL)	19.11±1.43	25.12±1.48	23.60±1.46**	**0.001**
8.	Cholesterol (mg/dL)	162.83±11.39	286.17±10.03	173.17±8.88**	**0.001**
9.	RBS (mg/dL)	80.33±3.96	98.56±4.31	100.78±4.22	0.421

Fig 4: Symmetrical bilateral alopecia and rat tail appearance in the 4 year old female Labrador retriever suffering from hypothyroidism)

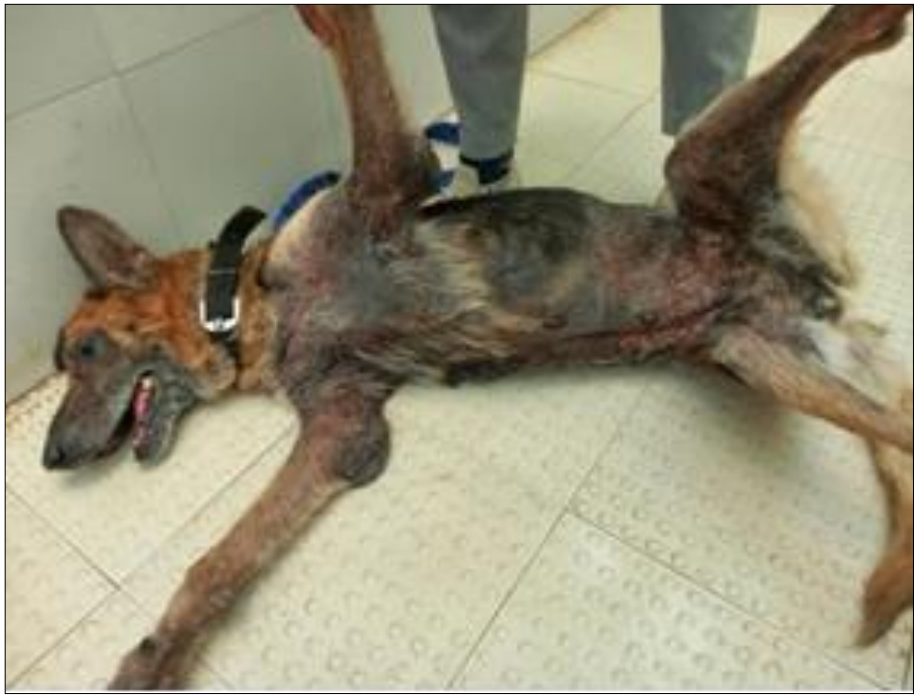


Fig 5: Hyperpigmentation and hyperkeratosis of the skin in a 6 year old German shepherd with hypothyroidism and secondary fungal infection

A **B** **C**

Fig 6: a,b,c Thinning of hair, dry and brittle hair coat, and failure of hair regrowth in the dogs suffering from hypothyroidism

A **B**

Fig 7: a, b, Classical Myxedema cutis seen in a 6year old male Labrador retriever suffering from canine hypothyroidism)

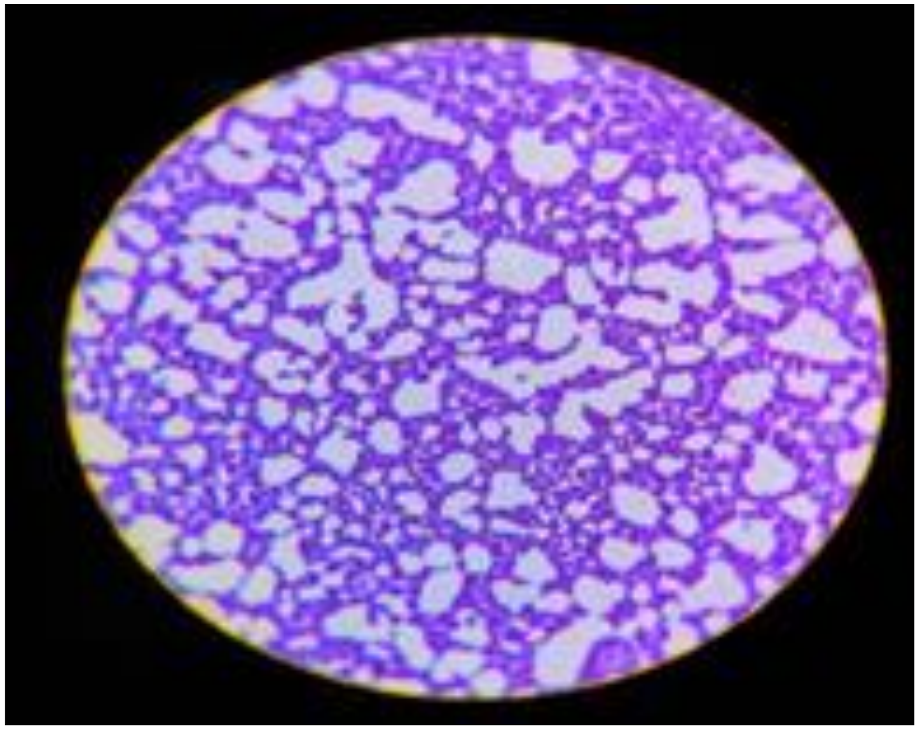


Fig 8: *Staphylococcus* spp. growth in pyoderma cases secondary to hypothyroidism

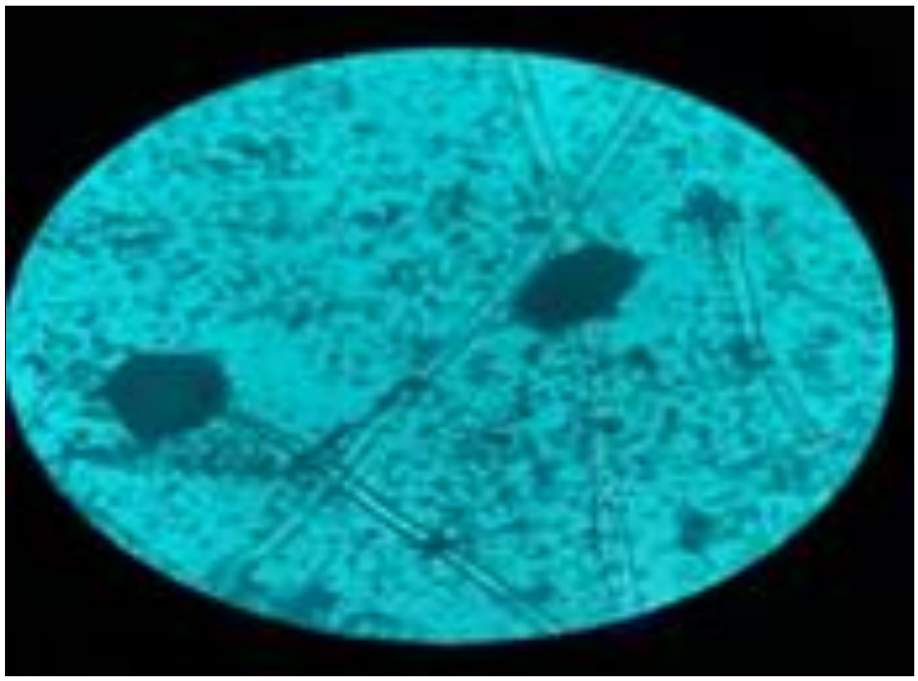
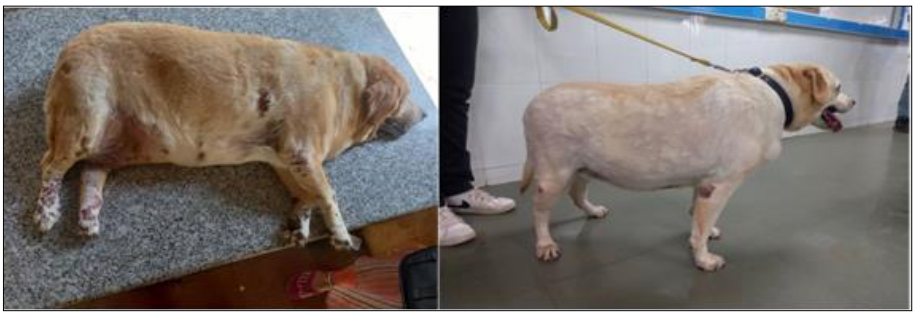


Fig 9: *Zygomycetes* spp. growth in mycotic dermatitis cases secondary to hypothyroidism by fungal culture and isolation

Fig 10: *Demodex* spp. in cases secondary to hypothyroidism)



A **B**

Fig 11: a, b, Obese and lethargic Labrador retrievers suffering from canine hypothyroidism)

Conclusion

The incidence of hormonal imbalance in dogs was 7.83 percent among the dermatological case load of the Veterinary College Complex, Anand. Hypothyroid dermatoses were the commonest one followed by hyperadrenocorticism and sex hormone endocrine dermatoses. The hypothyroidism was apparently more prevalent in the adult age group of dogs (6 to 9 years), comprising more Labrador Retrievers, nondescript dogs, and intact males. Typical dermatological signs such as bilaterally symmetrical alopecia, brittle hair and thin / sparse coat coupled with the characteristic physical signs such as rat tail, weight gain and cold intolerance in hypothyroidism would be the helpful clinical signs for the practitioners in arriving at a physical diagnosis. Chemiluminescence Immunoassay (CLIA) was used for hormonal estimation in healthy dogs and affected dogs before and after treatment. For the estimation of fT4 and TT4 CLIA can be relied upon but for the estimation of TSH, RIA Radioimmuno assay should be carried out further. Presence of anemia, leucocytosis with monocytosis and neutrophilia and hypercholesterolemia with elevated levels of aspartate aminotransferase were helpful supportive findings in the diagnosis of hypothyroidism. Levothyroxine @ 0.02 mg/kg BW along with supportive therapy was found to be effective in the clinical management of hypothyroid dermatoses.

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