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A comprehensive clinical study on canine hypothyroidism

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Abstract
In the present comprehensive study on canine hypothyroidism dogs presented with significant clinical signs such as dermatopathies and metabolic abnormalities were evaluated through a series of diagnostic protocol and later subjected for treatment. During this procedure almost all the dogs revealed non pruritic symmetrically bilateral alopecia along with alopecia at specific regions of wear and tear. The canine specific total thyroxine and free thyroxine was significantly low along with increased TSH levels which was a standard confirmation for hypothyroidism. Thirty hypothyroid dogs of various breed, age and gender were randomly divided into two groups with 15 each per treatment protocol. Group I dogs were managed with conventional levothyroxine and the other group dogs were additionally supplemented with oral equine placental extract for 30 days. Following treatment, clinical improvement with respective various dermatological abnormalities was seen in both the group dogs, but reached a complete clinical recovery by day 60 among the group II dogs. However, various thyroid hormones that was significantly altered on day 0 revealed to near normal by day 60 in all the dogs of both group I and II. Hence, the present investigation suggests the priority of supplementing antioxidants and other essential nutrients for a quick and complete recovery.

Keywords: Dermatological manifestation, dog, hypothyroid, levothyroxine, placenta extract

1. Introduction
Hypothyroidism was accounted for 32.9 percent in total dermatopathies (Costa *et al.*, 2016) [7] and one of the most commonly reported endocrinopathies (0.2 - 0.8 %) in dogs (Ferguson, 2007; De Bellis, 2011 and Mooney 2011) [14, 9, 18]. Dermatological manifestation was primarily recognised in dogs with hypothyroidism (80%), characterized by bilateral symmetrical alopecia with dull, dry hair coat, variable pigmentation, easy bruising, rat tail appearance and in delayed cases with secondary skin lesions (Srikala and Kumar, 2014) [25]. Estimation of free thyroxine (fT4) was reported to be better assessment for hypothyroidism evaluation in dogs since it was less commonly affected by drugs and concurrent illness (Celeska and Atanaskova, 2020; Bennaim *et al.*, 2022) [6, 3]. Diaz-Espineira *et al.* (2007) [10] described that TSH stimulation test was useful to differentiate hypothyroid dogs from euthyroid dogs, but substantial overlapping was also reported. Hegstad-Davies *et al.* (2020) [15] proved the breed specific variation of thyroid hormone levels in dogs. Hypothyroidism was effectively controlled by oral levothyroxine (0.02mg/kg BID) on an empty stomach and dogs with concurrent cardiac disease, levothyroxine dose was 0.005mg/kg BID (Hnilica and Patterson, 2016; Ashley, 2019 and Boretti, 2022) [16, 2, 4]. Satishkumar *et al.* (2023) [21] in their study reported the efficacy of placental extract supplement against canine alopecia. So, the current study was formulated to study and record the common clinical manifestations, to evaluate diagnostic procedures and to assess therapeutic regimens for hypothyroid dogs.

2. Materials and Methods
2.1 Study animals
A total of 30 dogs presented to Veterinary Clinical Complex, College of Veterinary Science, Rajendranagar with the following clinical manifestations indicative of hypothyroidism *viz.*, non - pruritic bilateral symmetrical alopecia, rat tailed appearance, hyper pigmentation of skin,

obesity, pot belly appearance, delayed wound healing, dry and brittle hair, numerous comedones, discolouration of coat and presence of puppy coat were taken for the study. Thyroid profile was evaluated and the hypothyroid dogs were taken for therapeutic study by randomly dividing into two groups *viz.*, group I and group II with 15 in each (Table 1).

2.2 Samples
The whole blood was collected into a clot activator coated sterile serum vials and the separated serum was aliquoted into labelled Eppendorf tubes and stored in deep freezer (-20 °C) for thyroid profile assessment by ELISA.

2.3 ELISA Kits
Serum levels of canine specific TT4 (Thyroxine), fT4 and cTSH (canine specific TSH) was measured by using ELISA kit with diagnostic sensitivity of 0.422 ng/ml, 0.938 pg/ml and 0.75 ng/ml, respectively. Detection limits were 0.703 - 45 ng/ml, 1.563 - 100 pg/ml and 1.25 - 80 ng/ml, respectively. Intra and inter assay covariance for all the assays were <8% and <10%. No significant cross reactions between thyroid hormones and analogues were observed. The standard curve was generated as per the kit standards (Ferguson *et al.*, 2001) [14] and estimation was carried out as per the manufacturer.

2.4 Therapeutic agents
Levothyroxine (Tab. Eltroxin 50, 100 and 150 µg, M/s. Glaxo Smithkline Pharmaceuticals Ltd., India or Tab. Thyrox 200µg, M/s. Macleods Pharmaceuticals Pvt Ltd., India) was used at the rate of 0.02mg/kg preferably on empty stomach. Placental extract (JBP EQ placental extract, 2 ml ampule, Japan) was used additionally in group II at the rate of 2 ml/10 kg body weight orally thrice weekly for two months.

Table 1: Study animals and treatment protocol

S. No.	Study animals (n = 30)	No. of dogs/group	Therapeutic trial	Dose
1.	Group I	15	Levothyroxine	@ 0.02 mg/kg, PO, SID
2.	Group II	15	Levothyroxine + placental extract	@ 0.02 mg/kg, PO, SID + 2 ml per 10 kg B.Wt orally, weekly twice

3. Results
3.1 Clinical observation
In canine hypothyroidism dermatological manifestations account for 86.67 percent cases (26/30), followed by metabolic in 46.67 percent (14/30), cardiovascular in 26.67 percent (8/30), reproductive in 6.67 percent (2/30), ophthalmic and neurological in 3.33 percent (1/30 each) dogs. The predominant dermatological signs recorded in the hypothyroid dogs of group I were pigmented skin, dry and rough coat (93.33 percent) followed by obesity (86.67 percent), lethargy and seborrhoea (80.00 percent). Whereas the group II dogs showed dry and rough coat (100 percent), pigmented skin, obesity and seborrhoea (93.33 percent), then lethargy (86.67 percent) and other general signs. Following treatment for 30 days, mild to moderate recovery noticed with respect to the pigmented skin, dry and rough coat, obesity and seborrhoea among dogs of both groups. Subsequently by day 60 group II dogs showed 100 percent recovery from lethargy, seborrhoea, rat tail appearance, bilaterally symmetrical and non-symmetrical alopecia, that was incomplete and partial recovery among group I dogs. The details are furnished in table 2, fig.1 and fig. 2.

Table 2: Evaluation of clinical signs in canine hypothyroidism (n=30)

S. No.	Significant manifestations	Group I n=15			Group II n=15		
		No. of animals showing manifestations			No. of animals showing manifestations		
		Day 0	Day 30	Day 60	Day 0	Day 30	Day 60
1.	Pigmented skin	14 (93.33%)	10 (66.67%)	7 (46.67%)	14 (93.33%)	4 (26.67%)	2 (13.33%)
2.	Dry and rough coat	14 (93.33%)	7 (46.67%)	5 (35.71%)	15 (100%)	7 (46.67%)	0 (26.67%)
3.	Obesity	13 (86.67%)	6 (40.00%)	4 (26.67%)	14 (93.33%)	7 (46.67%)	4 (26.67%)
4.	Lethargy	12 (80.00%)	3 (20.00%)	0 (0.00%)	13 (86.67%)	2 (13.33%)	0 (0.00%)
5.	Seborrhoea	12 (80.00%)	6 (40.00%)	3 (20.00%)	14 (93.33%)	8 (53.33%)	0 (0.00%)
6.	Rat tail appearance	11 (73.33%)	4 (26.67%)	2 (13.33%)	10 (66.67%)	4 (26.67%)	0 (0.00%)
7.	Circular alopecia	9 (60.00%)	5 (35.71%)	2 (13.33%)	8 (53.33%)	5 (35.71%)	3 (20.00%)
8.	Bilaterally symmet.alopecia	8 (53.33%)	2 (13.33%)	1 (6.67 %)	7 (46.67%)	2 (13.33%)	0 (0.00%)
9.	Bilaterally non symmetrical alopecia	7 (46.67%)	3 (20.00%)	1 (6.67 %)	8 (53.33%)	6 (40.00%)	0 (0.00%)
10.	Bradycardia	6 (40.00%)	2 (13.33%)	2 (13.33%)	5 (35.71%)	2 (13.33%)	1 (6.67 %)
11.	Delayed wound healing	5 (35.71%)	2 (13.33%)	1 (6.67 %)	3 (20.00%)	2 (13.33%)	1 (6.67 %)

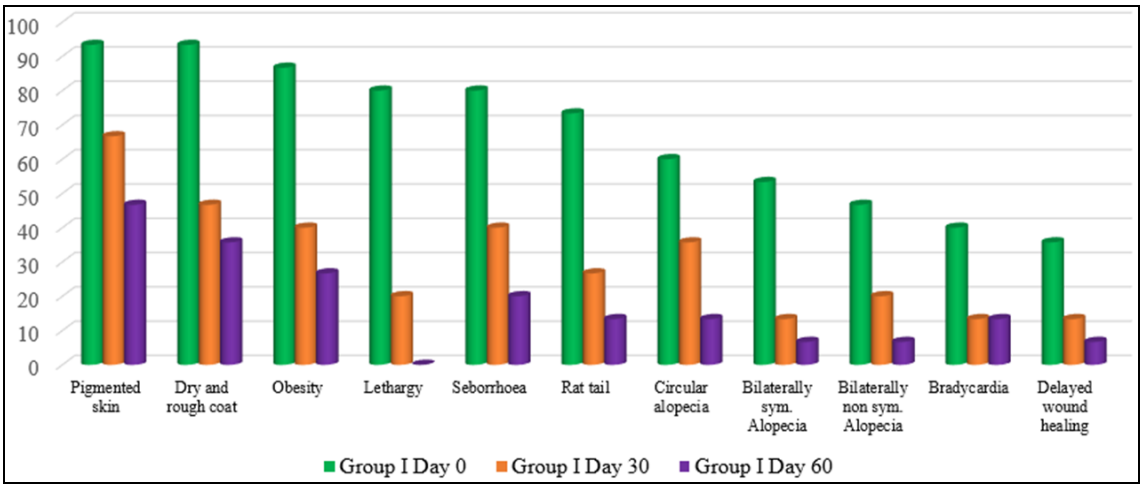

Fig 1: Cone chart showing evaluation of clinical signs in canine Hypothyroidism in Group I dogs before and after therapy.

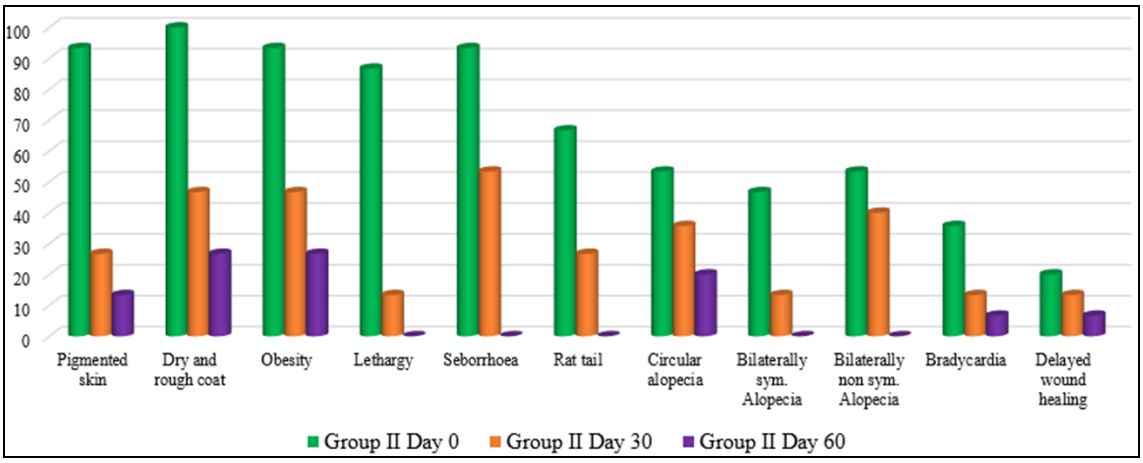

Fig 2: Cone chart representing evaluation of clinical signs in canine Hypothyroidism in Group II dogs before and after therapy.

3.2 Thyroid profile

The thyroid profile assessment *viz.*, canine specific TT4 (µg/dL), fT4 (ng/dL) and TSH (ng/ml) was carried out among suspected as well as healthy dogs through ELISA. Out of 46 suspected cases, 30 (65.21 percent) dogs that were confirmed for hypothyroidism were subjected for therapeutic evaluation. The values of TT4 (µg/dL) and fT4 (ng/dL) levels in healthy (4.03±0.32 and 1.43±0.11) and hypothyroid dogs of group I (1.02±0.04 and 1.03±0.03) and group II (1.12±0.05 and 0.96±0.02) were significantly different (p<0.05) from apparently healthy ones. The mean TSH (ng/ml) levels in ELISA was found significantly increased (p<0.001) in hypothyroid dogs of group I and II (4.92±0.25 and 5.05±0.34) when compared to healthy dogs (1.91±0.21). The details are presented in table 3.

Table 3: Thyroid profile in hypothyroid and healthy dogs

S. No	Parameters	Healthy	Group I	Group II
1	TT3 (ng/dL)	115.57±8.23	142.11±5.83*	116.47±0.46
2	TT4 (µg/dL)	4.03±0.32	1.02±0.04***	1.12±0.05***
3	fT4 (ng/dL)	1.43±0.11	1.03±0.03*	0.96±0.02*
4	TSH (ng/ml)	1.91±0.21	4.92±0.25***	5.05±0.34***

3.3 Therapeutic efficacy

The therapeutic evaluation was aimed to determine the effectiveness of the treatment protocols based on the observed clinical improvement, resolution of abnormal findings and the results of hormonal assays at the specified time points *viz.*, days 0, 30, and 60. Significant clinical improvement was noticed among both groups on day 30. By day 60, group II dogs showed complete recovery in multiple dermatological manifestations, emphasizing the effectiveness of the combined treatment that was not seen in group I cases. The study revealed significant improvement in thyroid function parameters over the course of the treatment. Both group I and II, there was a highly significant (p<0.001) increase in TT4 levels on day 60 (3.27±0.23 and 3.33±0.17), indicating a substantial improvement. Similarly, TSH levels decreased significantly (p<0.001) (1.97±0.23 and 2.18±0.26 ng/ml) on Day 60 among both the groups. Comparative analysis indicated that both group I and II showed substantial enhancements in thyroid parameters (Table 4).

Table 4: Mean serum thyroid profile of hypothyroid dogs of group I and II (n=30)

Parameters	Group IIa (n=15)			Group IIb (n=15)		
	Day 0	Day 30	Day 60	Day 0	Day 30	Day 60
TT4 (µg/dL)	1.02±0.04*	2.85±0.17	3.27±0.23***	1.12±0.05*	2.75±0.19	3.33±0.17***
fT4 (ng/dL)	1.03±0.03	1.31±0.13	1.42±0.13	0.96±0.02	1.33±0.06	1.52±0.04
TSH (ng/ml)	4.92±0.25***	3.19±0.25	1.97±0.23***	5.05±0.34***	3.90±0.29	2.18±0.26***

4. Discussion

Diagnosing hypothyroidism is often poses a challenge. So, it is recommended to collect proper history, clinical signs and assess thyroid profiles for a comprehensive diagnosis. Distinctive dermatological alterations, such as symmetrical bilateral hair loss, hyperpigmentation and the absence of itching, can manifest in dogs affected by canine hypothyroidism (Scarampella, 2011) [22]. The present study also documented 86.67 percent of dermatological manifestation in hypothyroid dogs. Thyroid hormones play a crucial role in ensuring the normal functioning of the skin and around 60% to 80% of dogs with hypothyroidism exhibit dermatological issues. The lack of thyroid hormones leads to decreased fibroblast activity and altered collagen metabolism, causing delayed wound healing and potential excessive fibrous tissue deposition after trauma (Credille *et al.*, 2001) [8]. The present study encountered dermatological, metabolic, cardiovascular, ophthalmic, reproductive and neuromuscular manifestation in canine hypothyroidism. Scott-Moncrieff (2007) [24] and Ettinger and Feldman (2010) [12] documented reduced metabolism and dermatological alterations, less commonly neurological, cardiovascular and female reproductive system affections in hypothyroid dogs. Alopecia commonly manifests itself in areas of pressure points (elbows and hips), entire length of tail (rat tail), the neck (starting at the collar) and the bridge of the nose. The very fine undercoat hairs may become more visible due to a preferential loss of guard hairs giving the appearance of a puppy coat (Miller *et al.*, 2013) [17]. The haircoat does not grow back after being clipped (Credille *et al.*, 2001) [8]. The common dermatological

signs recorded in the current study are in accordance with Scott *et al.* (2001) [23], Nelson and Couto (2009) [20] and Muntener *et al.* (2012) [19] who documented non-pruritic, non-inflammatory, bilaterally symmetrical alopecia and tragic face with additional cutaneous manifestations in hypothyroid dogs. The seborrhoea that was reported in hypothyroid dogs is in accordance with Castillo (2011) [5] documented dry or oily seborrhoea among 20 percent of hypothyroid dogs with or without generalized alopecia that could be due to extreme low levels of TT4 secretion. Lack of thyroid hormone impairs cell development in the epidermis and alters sebaceous gland secretion which could either leads to dry or oily seborrhoea (Nelson and Couto, 2009) [20]. In the present study both group I and II dogs, showed significant improvement in TT4 and TSH level among both the groups. Similarly, Dixon *et al.* (2004) [11] reported a favourable response to levothyroxine treatment among hypothyroid dogs with dermatitis lesions further lesions resolved within a six-week period of therapy. Alves *et al.* (2021) [7] reported rejuvenation of skin following the administration of levothyroxine treatment in primary canine hypothyroidism. Current study stated comparatively significant dermatological improvement on group II than I, it could be due to addition of placental extract in group II dogs. Placental extract could encourage hair growth in hypothyroid dogs (Satish Kumar *et al.*, 2023) [21]. Equine placental extract exhibits immunomodulatory and restorative properties, making it effective for managing diverse dermatological disorders (Fakhradiyev *et al.*, 2020) [13]. Further, placental extracts possess antioxidants, antimicrobial, anti-inflammatory properties, promote hair growth, and act as tissue regenerators and rejuvenation agents. Their findings support the use of placental therapy in managing dermatitis associated with endocrine disorders.

5. Conclusion

The current study recorded clinical features of hypothyroidism in dogs, emphasizing dermatological manifestations. Evaluating clinical symptoms alongside thyroid profile assessment is crucial for determining appropriate therapeutic interventions. The research highlights the effectiveness of oral levothyroxine and explores the potential role of placental extract supplementation, offering comprehensive insights into canine hypothyroidism management.

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