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Studies on Clinical Findings and Thyroid Profile in Hypothyroid Dogs Associated with Neuromuscular Disorders

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ABSTRACT

Background: The study aimed to appraise the clinical findings and thyroid profile changes in hypothyroid dogs associated with neuromuscular disorders.

Methods: The study comprised seven (7) healthy dogs (Group I) and 21 hypothyroid dogs with neuromuscular disorders (Group II). The serum concentration of Total Triiodothyronine (TT_3), Total Thyroxine (TT_4) and free Thyroxine (fT_4) was assessed using Radioimmunoassay (RIA), while Canine thyroid-stimulating hormone concentration (cTSH) was measured using a canine-specific TSH ELISA kit.

Result: The study reported that the neuromuscular signs associated with hypothyroidism were nystagmus (n=1/21, 4.76%), seizures (n=2/21, 9.52%), proprioceptive ataxia (n=3/21, 14.29%), head tilt (n=3/21, 14.29%), paraparesis (n=3/21, 14.29%), facial asymmetry (n=5/21, 23.81%), regurgitation due to megaesophagus (n=5/21, 23.81%) and tetraparesis (n=6/21, 28.57%). The mean serum concentration of TT_3, TT_4, fT_4 and cTSH in hypothyroid dogs associated with neuromuscular disorders was 0.89±0.04 (nmol/L), 9.45±0.94 (nmol/L), 7.72±0.37 (pmol/L) and 1.59±0.20 (ng/mL), respectively. The study found significantly ($p \leq 0.01$) lower TT_4 and fT_4 concentrations in hypothyroid dogs associated with neuromuscular disorders and significantly ($p \leq 0.01$) elevated cTSH levels compared to healthy dogs.

Key words: Canine thyroid stimulating hormone concentration (cTSH), Hypothyroidism, Neuromuscular dysfunction, Radioimmunoassay (RIA).

INTRODUCTION

Canine hypothyroidism is a prevalent hormonal disorder globally. The global prevalence has been reported as 0.20% (Dixon, 2001) and 0.80% (Catherine *et al.,* 2005). In India, Mumbai, Hisar and Punjab are prevalent areas for canine hypothyroidism, with a prevalence of 0.206%, 0.40% and 0.174 %, respectively (Pawar, 2009; Gulzar *et al.,* 2014, Kour *et al.,* 2020).

Thyroxine is crucial in cellular respiration, aiding in ATP production during aerobic metabolism by enhancing mitochondrial function. It also increases the activity of ATPase, which powers the ATP-dependent Na+/K+ pump. In hypothyroidism, reduced ATP production and diminished ATPase activity impair the Na+/K+ pump, disrupting axonal transport. Research has shown decreased axonal transport in the sciatic nerves of hypothyroid rats, suggesting that hypothyroidism may contribute to axonal degeneration and peripheral neuropathy (Jaggy *et al.,* 1994). Thus, hypothyroidism is linked to a range of neurological disorders, impacting cranial nerves, peripheral nerves and the central nervous system. Common neurological signs in hypothyroid dogs include facial nerve paralysis, megaesophagus, peripheral vestibular disease and lower motor neuron dysfunction (Lathan, 2012; Ettinger and Feldman, 2000).

In India, nuclear medicine and radioimmunoassay (RIA) have been widely used for thyroid hormone measurement in veterinary clinical settings (Dadke *et al.,* 2018; Roopali *et al.,* 2020; Galdhar *et al.,* 2021; Jayabhaye *et al.,* 2021; Galdhar *et al.,* 2022; Galdhar *et al.*, 2022; Salutgi *et al.,* 2023; Galdhar *et al.,* 2024; Galdhar *et al.,* 2024; and Alone *et al.,* 2025). However, reports on clinical findings and thyroid profile changes in hypothyroid dogs associated with neuromuscular signs are not available in India. This paper portrays the clinical findings and thyroid profile deviations in hypothyroid dogs related to neuromuscular disorders.

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MATERIALS AND METHODS

Statutory approval

The present study was initiated after permission from the Institutional Ethics Committee for Veterinary Clinical Research (IEC-VCR) and the Institutional Biosafety Committee (IBSC) of Mumbai Veterinary College, Maharashtra Animal and Fishery Sciences University (MAFSU), Mumbai-India.

Selection of hypothyroid dogs

The study comprised of seven (7) apparently healthy dogs (Group I) and 21 hypothyroid dogs with neuromuscular disorders (Group II). A total of 21 dogs (Group II) from different breeds, suspected of having clinical hypothyroidism related to neuromuscular disorders, were ethically enrolled at the clinical facility of Mumbai Veterinary College, Parel-Mumbai, for thyroid profile assessment. This group consisted of 10 males and 11 females, with an average age of 6.83±0.68 years and an average body weight of 21.26±2.42 kg, respectively.

Hormonal analysis

Blood samples were obtained from each dog by the cephalic or saphenous veins. Serum samples proposed for thyroid profile analysis were stored at -20°C until testing. Total Triiodothyronine (TT_3), Total Thyroxine (TT_4) and free Thyroxine (fT_4) were measured using commercial RIA kits designed for human use (Immunotech s.r.o., Radiova 1122/1, 102 00 Prague 10, Czech Republic, distributed by Beckman Coulter Company, Mumbai, India). Canine thyroid-stimulating hormone (cTSH) was measured using canine canine-specific TSH ELISA kit (Wuhan Fine Biotech Co., Ltd., Hubei, China). The analysis was performed at the Radio Isotope Laboratory, Mumbai Veterinary College, Mumbai, India. All the hormonal analysis assays were carried out by following the standard protocol provided by the kit manufacturer. Each sample was analysed in duplicate to ensure paired observations. To validate the assay, quality control measures, including the magnitude of control samples and recovery percentages, were monitored.

Diagnosis

Diagnosis of hypothyroidism was made based on altered thyroid profile and response to replacement therapy of thyroxine.

Statistical analysis

The mean and standard error for each parameter of the collected data were computed and statistically analysed for comparison, following the methods outlined by Snedecor and Cochran, (2004). Additionally, a nonparametric statistical approach was employed to analyse the results.

RESULTS AND DISCUSSION

The neurological signs observed in hypothyroid dogs (Group II) in this study are summarized in Table 1 and Fig 1.

The neurological signs recorded were nystagmus (n=1/21, 4.76%), seizures (n=2/21, 9.52%), proprioceptive ataxia (n=3/21, 14.29%), head tilt (n=3/21, 14.29%), paraparesis (n=3/21, 14.29%), facial asymmetry (n=5/21, 23.81%), regurgitation due to megaesophagus (n=5/21, 23.81%) and tetraparesis (n=6/21, 28.57%). Similar

Table 1: Neurological signs in hypothyroid dogs.

Neurological sign	No. of dogs	% of dogs
Nystagmus	1	4.76
Seizures	2	9.52
Proprioceptive ataxia	3	14.29
Head tilt	3	14.29
Paraparesis	3	14.29
Facial asymmetry	5	23.81
Regurgitation/ megaoesophagus	5	23.81
Tetraparesis	6	28.57

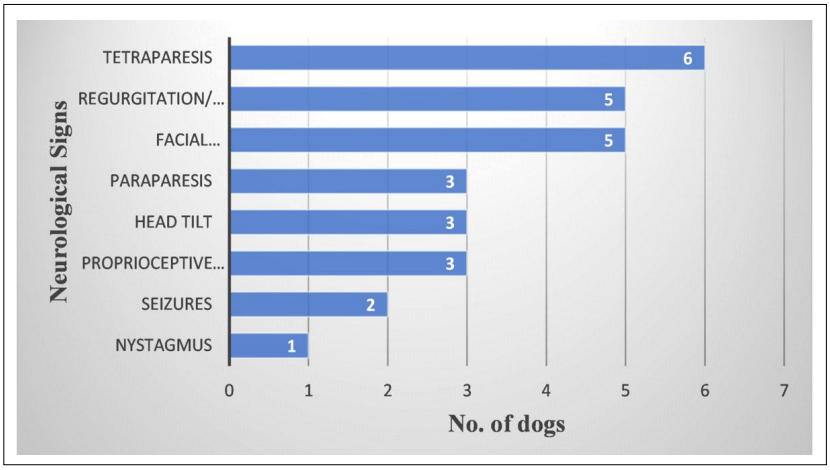

Fig 1: Neurological signs in hypothyroid dogs.

neurological signs have been reported in previous studies by Bichsel *et al.* (1988), Jaggy *et al.* (1994), Panciera, (1994), Fracassi and Tamborini, (2011) and Kırbaş, (2020).

The study found clinical signs of classical hypothyroidism in five dogs (n=5/21), including lethargy, obesity, rough coat, sparse coat and skin infection, suggesting neuromuscular symptoms may be the primary manifestation. The exact pathophysiology of hypoth yroidism-related neuromuscular disorders is unclear. Ettinger and Feldman, (2000) suggested mucop olysaccharide accumulation, impaired axonal transport, or atherosclerosis may cause neurological signs. Nelson and Couto, (2019) suggested that segmental demyelination and axonopathy, affecting both central and peripheral nervous systems, could cause neurological manifestations without typical hypothyroidism symptoms. Hypothyroid neuropathy, a condition characterized by energy metabolism deficits, disrupts axonal transport and Schwann cell function, leading to cranial nerve issues and compression caused by myxedematous deposits in the head and neck tissues (Jaggy *et al.,* 1994; Panciera, 1994 and Romão *et al.,* 2012). Reduced vascular perfusion to the inner ear might also contribute to the development of facial neuropathies in hypothyroid dogs (Vitale and Olby, 2007).

The serum concentration of cTSH was measured using a canine-specific TSH ELISA kit, while TT_3, TT_4 and fT_4 concentrations were estimated using an RIA kit. Both assays were conducted on serum samples of healthy (n=07) and hypothyroid dogs associated with neuromuscular disorders (n=21). All recommended quality control parameters, including the magnitude of control samples provided with the kits and percent recovery, were within the prescribed limits. The standard curve of the assays was plotted and the thyroid hormone concentrations were interpolated from the standard curve.

The mean, interquartile range (*i.e.*, 25th to 75th percentile) and median of thyroid hormones in healthy dogs and hypothyroid dogs associated with neuromuscular disorders are presented as a box plot (Fig 2 to 5).

The mean concentrations of TT_3, TT_4, fT_4 and TSH in healthy dogs were 1.08±0.14 (nmol/L), 20.12±1.40 (nmol/L), 14.77±0.83 (pmol/L) and 0.25±0.04 (ng/mL), respectively. The mean concentrations of TT_3, TT_4, fT_4 and TSH in hypothyroid dogs associated with neuromuscular

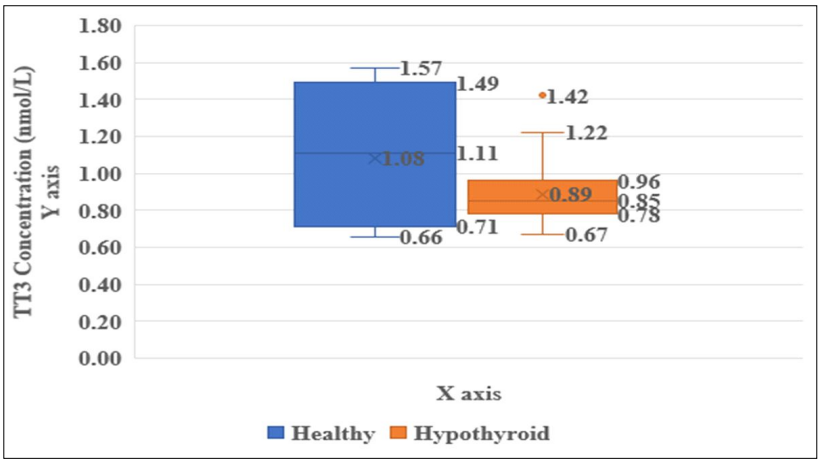

Fig 2: Box plot comparison of TT_3 (nmol/L) between healthy and hypothyroid dogs.

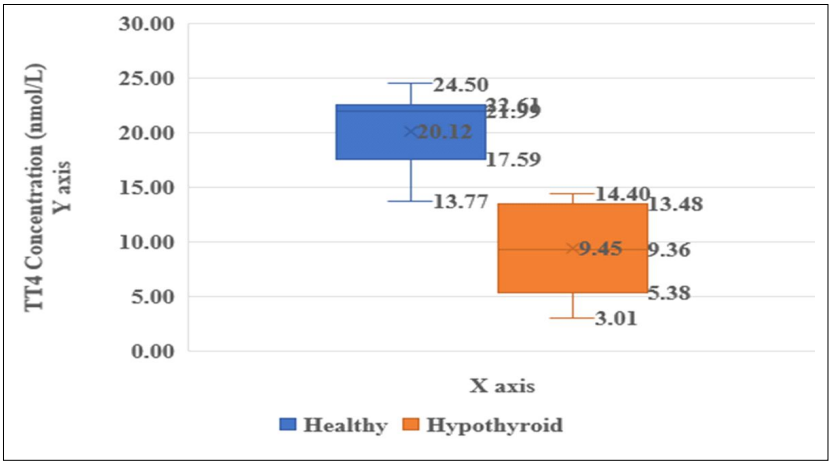

Fig 3: Box plot comparison of TT_4 (nmol/L) between healthy and hypothyroid dogs.

disorders were 0.89±0.04 (nmol/L), 9.45±0.94 (nmol/L), 7.72±.37 (pmol/L) and 1.59±0.20 (ng/mL), respectively.

The box plot (Fig 2) represents the range of TT_3 values (0.67 to 1.22 nmol/L), with the interquartile range between 0.78 and 0.96 nmol/L and the median TT_3 concentration at 0.85 nmol/L in hypothyroid dogs. In the box plot (Fig 3), the range of TT_4 values spans from 3.01 to 14.40 nmol/L, with an interquartile range of 5.38-13.48 nmol/L and the median concentration at 9.36 nmol/L in hypothyroid dogs. For fT_4 concentrations, the box plot comparison between healthy and hypothyroid dogs is presented in Fig 4. The box plot indicates the range of values from 5.13 to 10.60 pmol/L, with the interquartile range between 6.38 and 8.82 pmol/L and a median fT_4 concentration of 7.80 pmol/L in hypothyroid dogs. The cTSH concentrations box plot comparison between the two groups is presented in Fig 5. The range of cTSH values spans from 0.11 to 2.98 ng/mL, with an interquartile range of 1.08-2.53 ng/mL and the median TSH concentration in hypothyroid dogs was 1.45 ng/mL.

In the hypothyroid dogs associated with neuromuscular disorders, the mean concentrations of TT_3, TT_4 and fT_4 were below the reference ranges established by Galdhar *et al.* (2022) for healthy dogs. A highly significant ($p \leq 0.01$) difference was observed in serum total thyroxine and free thyroxine levels between the groups, while a non-significant difference was found in TT_3 concentrations. Similar findings were reported by Higgins *et al.* (2006) and Alone *et al.* (2025). The lack of a significant difference in TT_3 levels between healthy and hypothyroid dogs supports the observations of Kantrowitz *et al.* (2001), who queried about the sensitivity and accuracy of TT_3 for diagnosing hypothyroidism.

The mean cTSH concentration in the hypothyroid group was found to be higher than the reference range reported by Kemppainen and Behrend, (2001); Gulzar *et al.* (2014), Kour *et al.* (2021) and Boretti *et al.* (2022) for healthy dogs. A significant ($p \leq 0.01$) difference in cTSH concentrations was noted between healthy and hypothyroid groups, with the hypothyroid dogs showing elevated TSH levels. This aligns with findings from Bonagura and Twedt, (2013), Pawar, (2009) and Fernandez and Seth, (2016), who also reported significant increases in TSH in hypothyroid dogs.

The thyroid gland's primary function is to produce active thyroid hormones. Any structural or functional abnormalities in the thyroid gland or hypothalamic-pituitary-thyroid axis,

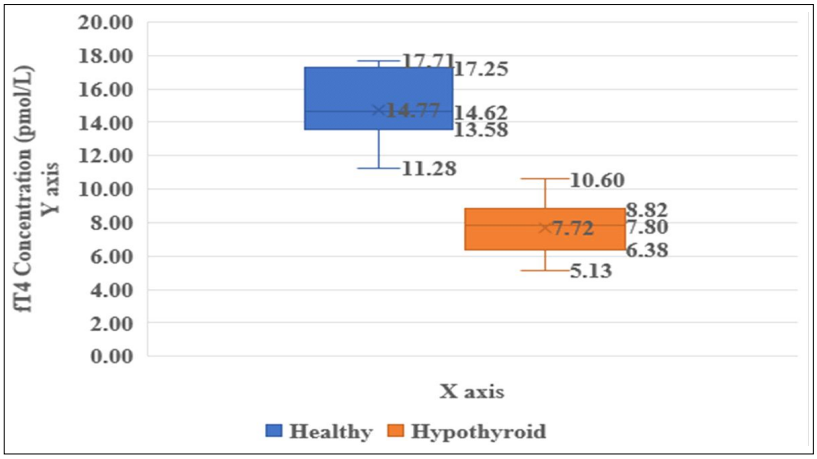

Fig 4: Box plot comparison of fT_4 (pmol/L) between healthy and hypothyroid dogs.

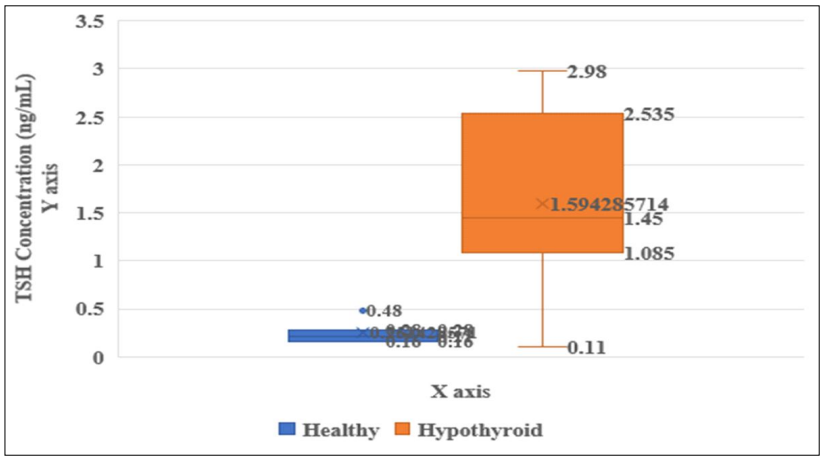

Fig 5: Box plot comparison of cTSH (ng/mL) between healthy and hypothyroid dogs.

leading to reduced thyroid hormone production, result in hypothyroidism. Depending on the location of the defect, hypothyroidism is classified as primary, secondary, or tertiary. Primary hypothyroidism is due to issues within the thyroid gland, while secondary and tertiary hypothyroidism occur due to dysfunctions in the pituitary and hypothalamus, respectively (Nelson and Couto, 2019; Ettinger and Feldman, 2000). In primary hypothyroidism, subnormal levels of thyroid hormones lead to decreased negative feedback on pituitary TSH synthesis and release, causing elevated circulating TSH concentrations in affected dogs (Dixon, 2001).

In this study, 4 dogs in the hypothyroid group had TSH concentrations within the reference range, representing 19.04% of the hypothyroid dogs. This finding is following Scott-Moncrieff *et al.* (2002), who found that 30% of hypothyroid dogs had TSH levels within the reference range, likely due to the inability of the TSH assay to detect all circulating TSH isoforms.

CONCLUSION

Hypothyroidism in dogs is linked to neurological symptoms, viz. tetraparesis, megaesophagus, facial asymmetry, paraparesis, head tilt, proprioceptive ataxia, seizures and nystagmus. These clinical signs should raise suspicion for hypothyroidism. Dogs with hypothyroidism displayed significant changes in their thyroid profile. They had significantly lower ($p \leq 0.01$) total thyroxine and free thyroxine concentrations, while their thyroid-stimulating hormone levels were significantly ($p \leq 0.01$) elevated.

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Conflict of interest

The authors declare that there is no conflict of interest.

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