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Incidence of Canine Atopic Dermatitis (CAD) in Mizoram

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ABSTRACT

The study conducted to evaluate the incidence of canine atopic dermatitis in Mizoram and to assess its clinical features according to the diagnostic criteria of the disease. The dogs brought with the history of recurrent pruritus and fulfilling clinical criteria given by Favrot *et al*. (2010) were subjected for various diagnostic techniques. After exclusion of other pruritic dermatological problems such as flea allergy dermatitis, scabies and demodecosis, intradermal test with environmental allergens was performed on atopic dogs. They were later evaluated for distribution of clinical lesions and severity measured by Canine Atopic Dermatitis Extent and Severity Index. Evaluation of serum IgE using Canine IgE Rapid test kit and serum Interleukin-31 levels using the Serum Interleukin-31 ELISA kit was done. Blood samples were analyzed for hemato-biochemical parameters. The incidence rate of canine atopic dermatitis was 3.27% (20/612) and the age group of 6 months to 3 years were mostly affected. Incidence was higher in female dogs. Hematological study revealed significant changes in total leukocyte count, leukocytosis, neutrophilia and eosinophilia. For biochemical parameters, there were no significant changes in blood urea nitrogen, creatinine, alanine transaminase, alkaline phosphatase, total protein and albumin. Serological estimation of immunoglobulins and interleukin revealed significant ($p<0.05$) increase in levels of IgE and interleukin-31 in the serum of atopic dogs. The dogs showed positive intradermal test to house dust, house dust mite and some pollen.

HIGHLIGHTS

- Multifactorial disease with recurrent pruritus as hallmark sign.
- Immunoglobulins IgE and interleukin-31 can be used as a diagnostic marker for canine atopic dermatitis along with intradermal skin test.

Keywords: Erythema, IgE, IL-31, IDT, Pruritus

Canine atopic dermatitis (CAD) is a chronic, allergic skin disease associated with IgE-mediated reactions to environmental allergens (Halliwell, 2006). CAD affects up to 10% of dogs (Ka *et al*., 2014), and it is reported that pure-bred dogs have a greater probability of expressing atopy and allergic dermatitis than mixed breed dogs (Bellumori *et al.*, 2013). Pruritus is the hallmark of CAD and erythema is often prime lesion present in the atopic dogs (Griffin and DeBoer, 2001). The lesions are distributed on face, ventrum, trunk, feet, ear pinnae and flexural fold (Varshney *et al.,* 2013). It thereby constitutes a serious medical problem in veterinary medicine and cause great distress to patients and their owners. Atopic dermatitis is usually a life-long disease that can be managed but rarely cured. Atopy is characterized by tendency to produce IgE

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antibodies in response to low doses of allergens, usually proteins delivered by inhalation or ingestion and as a consequence, to develop typical symptoms of asthma, rhino-conjunctivitis or allergic skin disease (World Allergy Organization, 2003). Hence, the study has been taken up to find out the incidence of canine atopic dermatitis and its early diagnosis for prevention and control.

MATERIALS AND METHODS

The study included 612 dogs that were brought to Teaching Veterinary Clinical Complex (TVCC) at College of Veterinary Sciences and A.H, Selesih, Aizawl, Mizoram during the period of August 2017 to March 2018, affected with various skin affections along with history of reoccurring persistent pruritus, erythema and alopecia.

Detail dermatological examination and laboratory examinations were carried out for the dogs brought with the history of recurrent pruritus to rule out other similar dermatological conditions.

All the suspected cases of CAD, fulfilling clinical criteria given by Favrot *et al*. (2010) were subjected to intradermal test (IDT) with environmental allergens (pollens, house dust and house dust mite) and interpreted according to accepted criteria to confirm the allergen specific IgE production as per Hillier and DeBoer (2001).

Estimation of IgE antibodies in serum was done using Canine IgE Rapid test kit. Evaluation of Interleukin-31 levels was done in each dog using the Serum IL-31 ELISA kit following manufacturer protocol. Six apparently healthy dogs irrespective of age, sex and breed were chosen randomly to act as control group for the present study.

Complete Blood Count (CBC) was carried out with the help of semi-automated blood analyser (Melet Schloesing 4e, France). The haematological parameters such as hemoglobin (Hb), packed cell volume (PCV), total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC) and thrombocyte count were considered.

The serum samples were analyzed for biochemical parameters like blood urea nitrogen, creatinine, total protein, albumin and glucose with the help of automated fuji blood analyzar (automated fuji drichem blood analyzar, Japan).

Statistical analysis of the data was done using statistic software SPSS 16.0. Data pertaining to hematological, biochemical profiles and serological profiles was analyzed by one-way ANOVA technique to test the significance of means as per the method described by Snedecor and Cochran (1994).

RESULTS AND DISCUSSION

Out of 612 cases, 20 dogs (3.27%, 20/612) were confirmed as canine atopic dermatitis by ID test (Table 1) which was in agreement with Halliwell and Schwartzman (1971). IDT performed on CAD affected dog is shown in Fig 1. All 20 dogs reacted to the positive control (histamine) and had a low level of pruritus at the inoculation site but without other secondary symptoms. The majority of dogs had immediate positive skin reactions, with appearance of a wheal and nodule at the injection site, to the house dust mite, *Dermatophagoides farinae* (100%, 20/20) which is also found by Nagy and Pop (2008). The study revealed that 80% dogs above six months were most commonly affected than younger age group (2-6 months).

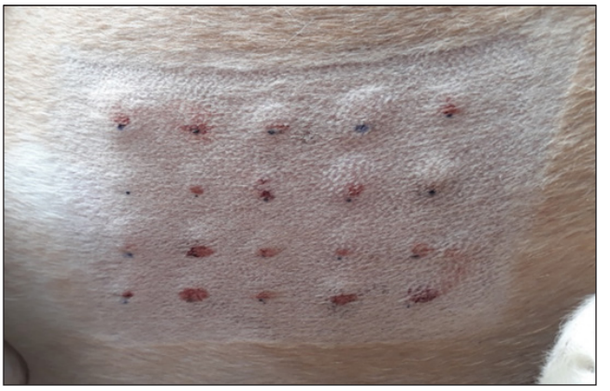

Fig 1: Intradermal allergen test in an atopic dog

In the present study, 40% (8/20) CAD cases were observed in male dogs and 60% (12/20) in female dogs. Breed-wise incidence study revealed that highest incidence of CAD was observed in Pug and mixed (5/20-25% each) followed by Labrador retriever (3/20-15%), English bulldog (2/20-10%), Saint Bernard (2/20-10%), Great Dane (2/20-10%) and Beagle (1/20-5%). Canine atopy is reportedly more common in females than in males (Scott *et al.,* 2001), although some studies showed no sex predilections (Bizikova *et al*., 2015). In the present study, females were

Table 1: Mean and total CADESI lesion score for Erythema, Excoriation and lichenification in dogs affected with CAD (n=20)

CADESI-4 (ICADA 2013)		Erythema		Excoriation		Lichenification	
Body Locations		**AVG. CADESI Score**	**Total CADESI Score**	**AVG. CADESI Score**	**Total CADESI Score**	**AVG. CADESI Score**	**Total CADESI Score**
Perilabial Area (left and right combined)		1.50	27	0.72	13	0.5	5
Medial Pinnae (concave pinnae)	Left	1.89	34	1.11	20	0	2
	Right	1.89	34	1.11	20	0	2
Axillae	Left	1.61	29	1.17	21	1	10
	Right	1.61	29	1.17	21	1	10
Front Paws (dorsal and palmar sides combined)	Left	1.83	33	1.22	22	1	8
	Right	1.83	33	1.22	22	1	8
Hind Paws(dorsal and plantar sides combined)	Left	0.83	15	1.17	21	0.5	3
	Right	0.83	15	1.17	21	0.5	3
Thorax	Left	0.94	17	1.44	26	0	4
	Right	0.94	17	1.44	26	0	4
Flanks	Left	0.89	16	1.28	23	0.5	4
	Right	0.89	16	1.28	23	0.5	4
Flexural areas	Left	0.94	17	1.17	21	0.5	7
	Right	0.94	17	1.17	21	0.5	7
Thigh	Left	0.50	9	1.17	21	0.5	3
	Right	0.50	9	1.17	21	0.5	3
Groin		1.50	27	1.00	18	1	13
Anogenital area		0.39	7	0.83	15	0	1
Ventral Tail		0.83	15	0.89	16	0.5	5

over-represented but this does not mean a sex predilection if we compare it to the dog population in Mizoram where this ratio is the same. In breed wise incidence highest cases of CAD was observed in pure breed than mixed, which is in agreement with Bellumori *et al.* (2013) who also reported that pure-bred dogs have a greater probability of expressing atopy and allergic dermatitis than mixed bred dogs.

Pruritus (100%) was the most predominant sign of atopic dermatitis, observed in the study. The major distribution of different lesions on body is shown in Table 1. The erythema was mostly present in ear pinnae followed by, front paws, right and left axilla, groin and perilabial area among the twenty sites on the body also reported by Brar *et al*. (2017) (Fig. 2 & 3). The excoriation was found predominantly in thorax region, flank region followed by front paws, left axilla as well as right axilla (Table 1). Minimum excoriation was observed at perilabial area preceded by anogenital area and at ventral tail. The lichenification was the least observed lesion among the three. It was mostly present in groin and axilla. The pruritus and erythema was the major clinical signs also observed by Favrot *et al.* (2010). The pruritus and erythema in the CAD affected dogs were produced due to degranulation of IgE bound mast cells when re-exposure to specific allergens resulted in production of proteolytic enzymes, histamine, bradykinins, and other vasoactive amines, leading to inflammation (Scott *et al.,* 2001). The excoriation/self-induced alopecia has been caused due to intense pruritus and deep scratching. The lichenification was due to activation of mast cells within the dermis that induces the release of pro-inflammatory mediators and cytokines. These factors promote the recruitment of immune cells having JAKs on their surface.

There was no significant difference of Hb, PCV and TEC in between CAD and healthy dogs (Table 2). TLC count (17.58±0.87 m/mm^3) in diseased group revealed a significant ($p<0.05$) increase as compared to healthy control (13.41±0.96 m/mm^3). Neutrophilia (77.35±1.14%) and eosinophilia (4.72±0.21) were observed in atopic dermatitis affected dogs as compared to healthy ones (72.88±1.24 % and 2.50±0.43). Leukocytosis was

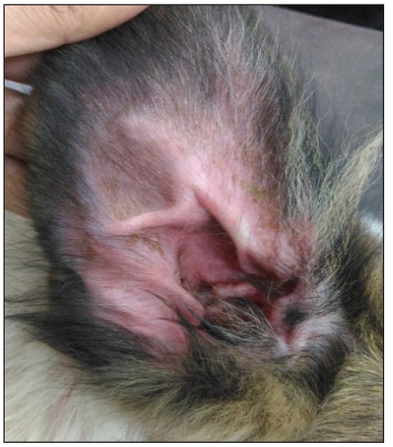

Fig. 2: Erythema in ear pinnae

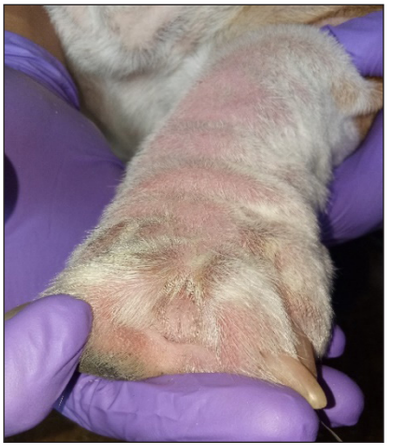

Fig. 3: Erythema in forelimb

observed in present study, which corresponded with the observations of Joni *et al.* (2003) and Sharma and Gupta (2005). Leukocytosis could be due to cellular and hormonal immune response in allergic dermatitis. The leukocytosis could also have resulted from toxins released due to tissue damage or necrosis produced by inflammation or from secondary bacterial infection as also mentioned by Gupta and Prasad (2001).

Table 2: Haematological status in CAD affected dogs in comparison to healthy dogs

Parameters	Healthy (n=6)	CAD affected dogs (n=20)
Hb (g/dl)	13.22±0.63	14.23±0.55
PCV (%)	39.33±2.01	41.02±1.79
TEC (M/mm^3)	6.71±0.25	9.28±1.65
TLC (m/mm^3)	13.41 ±0.96	17.58±0.87
THR (lakhs)	290.50±15.88	230.39±21.00
L (%)	21.02±1.13	13.97±1.05
M (%)	3.60±0.27	3.95±0.24
N (%)	72.88±1.24	77.35±1.14
E (%)	2.50±0.43	4.72±0.21

Neutrophilia was observed in atopic dermatitis might be due to primary and secondary infections due to heavy bacterial load which might result in mobilization of marginal and bone marrow granulocytic pool as also reported by Schalm (1963). Lymphocytosis was also observed in the present study, which is in agreement with finding of Latimer (1995). Eosinophilia observed in the present study might be due to hypersensitivity reaction because of raised histamine concentration that causes release of eosinophils in the blood circulation. The result is in agreement with Brar *et al*. (2017).

There were no significant changes in BUN (9.69±0.77 mg/dl), creatinine (0.98±0.07 mg/dl), Total protein (6.59±0.15 g/dl) and albumin (2.98±0.05 g/dl) and glucose (79.50±3.83 mg/dl) level of infected dogs as compared to healthy one (Table 3). These observations corroborate with those of Sharma and Gupta (2005); Dip *et al.* (2013) and Kapun *et al*. (2014) who also did not find any biochemical changes.

Table 3: Biochemical status in CAD affected dogs in comparison to healthy dogs

Parameters	Healthy (n=6)	CAD affected dogs (n=20)
BUN (mg/dl)	10.03±1.11	9.69±0.77
Creatinine (mg/dl)	0.93±0.07	0.98±0.07
TP (g/dl)	6.22±0.18	6.59±0.15
Alb (g/dl)	3.28±0.21	2.98±0.05
Glu (mg/dl)	76.00±4.97	79.50±3.83

Almost all the dogs showed positive or borderline positive result indicating the presence of total IgE above 10 µg/mL (Fig. 4). The elevated levels of IgE in CAD affected dogs were in agreement with (Scott *et al.,* 2001; Walaa *et al.,* 2008 and Brar *et al*., 2017). The high production of IgE might be due to the allergen's absorption into the body by

percutaneous route into the skin leading to degranulation of mast cells and excessive production of histamine into the circulation.

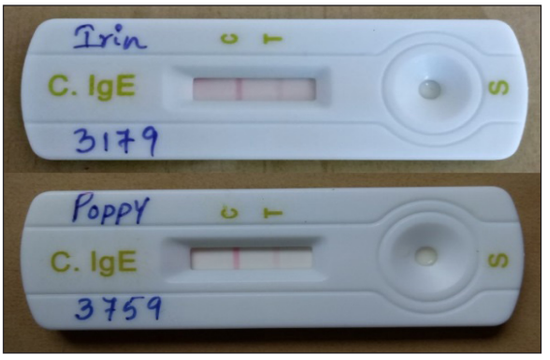

Fig. 4: Canine IgE test Kit showing Strong Positive tests

There was a significant increase in level of canine IL-31 in diseased animal when compared with healthy control. The mean of canine IL-31 in diseased dogs (216.82±18.97 pg/ml) was significantly ($p<0.05$) higher than healthy control (111.06±7.09 pg/ml) (Table 4). IL-31, preferentially produced from TH2 cells, is a potent pruritogenic cytokine which plays a major role in atopic dogs as pruritus is the hallmark sign of CAD. These observations substantiate with those of Gonzales *et al*. (2013) and Furue *et al.* (2018).

Table 4: IL-31 status in CAD affected dogs in comparison to healthy dogs

Parameter	Healthy (n=6)	CAD affected dogs (n=20)
IL-31 (pg/ml)	111.06±7.09	216.82±18.97

CONCLUSION

In conclusion, serological estimation of immunoglobulins IgE and interleukin-31 are to be used as a diagnostic marker for canine atopic dermatitis along with intradermal skin test. The dogs showed positive IDT to house dust, house dust mite (HDM) and some pollen in the present study.

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