Journal of Animal Research: v.7 n.3, p. 507-513. June 2017

DOI: 10.5958/2277-940X.2017.00075.4

Clinico-pathological Studies on Atopic Dermatitis in Dogs

Rasmeek Kaur Brar*, P.S. Dhaliwal, Ashwani Kumar, Sushma Chhabra and S.K. Uppal

Department of Veterinary Medicine, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, INDIA

**Corresponding author: RK Brar; Email: rasmeek.brar@gmail.com*

Received: 11 Dec., 2016 **Revised:** 05 May, 2017 **Accepted:** 07 May, 2017

ABSTRACT

The present study was conducted to record the clinico-haematological, biochemical and serological changes in atopic dermatitis in canines amongst the various dermatoses cases presented at the Teaching Veterinary Clinical Complex, GADVASU, Ludhiana. Fifty two atopic dermatitis affected dogs were enrolled in the study with chief complaint of intense pruritus, erythema and alopecia. Prevalence of atopy among various dermatoses was 27.90% which mainly occurred during monsoon. Labrador, Toy breeds and German Shephard of 1-3 years of age were affected more. Dogs suffering from atopic dermatitis showed pruritus (100%), erythema (82.69%), alopecia (75.00%), hyperpigmentation (36.00%), scales/crusts (25.00%), lichenification (21.15%) and excoriation (19.60%). The lesions in atopic dermatitis were mainly located at groin (88.40%), abdomen (78.80%), neck (76.90%), perioccular region (75.00%), axilla (71.10%), muzzle and paws (69.20%), ear pinna (67.30%), limbs (48.07%) and tail (7.60%). Haematobiochemical study revealed significant changes in TLC, neutrophilia, eosinophilia and total protein. Serological estimation revealed significant increase in levels of IgE in the serum of atopic dogs.

Keywords: Atopy, Allergy, dermatitis, dogs

Canine Atopic Dermatitis (CAD) has been defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features. It is associated most commonly with IgE antibodies to environmental allergens (Halliwell*,* 2006). Atopy comes from Greek word meaning "strange disease" is a term that has long been applied to describe allergic asthma, hay fever and atopic dermatitis (Nambi and Kavitha, 2013). Altered skin barrier dysfunctions have shown to be the main factor involved in the pathogenesis and predisposition of atopic dermatitis (AD). Numerous other factors that are known to play a role include defective epidermal barrier function, processing of allergens by epidermal Langerhans' cells, polarization of T-lymphocyte cytokine responses, increased releasability of cutaneous mast cells, and susceptibility to secondary bacterial and yeast infections. Environmental allergens like house dust mites, pollens from trees, weeds, grass, mould spores, epidermal and insect antigens and miscellaneous antigens such as kapok have also been suggested to be involved in the pathogenesis of canine atopic disease (Hill and DeBoer, 2001).

The exact prevalence of AD is not known, but it is suggested that approximately 10% of the canine population is affected by this skin disease (Scott *et al.,* 2001) and pruritus is the hallmark of this disease. In one of the few studies in India, atopic dermatitis was found to be the most common among all allergic dermatitis in dogs. (Sharma *et al.*, 2015a). The typical age of onset is 6 months to 3 years, though it is possible that signs will present in dogs less than 6 months and greater than 7 years old (Saridomichelakis *et al.,* 1999). Clinical signs of CAD can be both seasonal and non-seasonal depending on which allergens are involved. The diagnosis of canine AD is based upon clinical history, physical examination, characteristic clinical features with exclusion of other diseases with a similar clinical presentation and diagnostic tests including allergen-specific IgE serology (ASIgES). AD is usually a life-long disease that can be controlled but rarely cured. Aim of the present study is to know the clinical presentation and haemato-biochemical alteration in atopic dogs.

MATERIALS AND METHODS

The study included total 186 dogs which were brought to Teaching Veterinary Clinical Complex (TVCC) at Guru Angad Dev Veterinary and Animal Sciences University (GADVASU), Ludhiana, affected with various skin affections along with history of reoccurring persistent pruritus, erythema and alopecia. They were subjected to detailed physical, clinical and dermatological examination. Number of dogs suffered from atopic dermatitis was categorized according to the age, sex, breed and season of disease occurrence. The diagnosis of atopic dermatitis was based on skin scrapings, hair specimens, impression smears, bacterial and fungal cultures to rule out other pruritic skin infections that mimic atopic dermatitis. Diagnostic criteria proposed by Favrot *et al.* (2010) with one additional feature (Elevated allergic specific IgE, Willemse (1986, 1988) was followed and includes:

- ❒ Onset of signs under three years of age
- ❒ Dog living mostly indoors
- ❒ Gluco-corticoid responsive pruritus
- ❒ Pruritus before skin lesions
- ❒ Affected front feet and concave (inner surface of ear pinnae)
- ❒ Non- affected ear margins (affected ear margins most consistent with sarcoptes)
- ❒ Non-affected dorsolumbar area (affected dorsolumbar area most consistent with flea allergic dermatitis).

Scoring of dermatological lesions was done as follows: (Fontaine and olivry, 2001; Puigdemont *et al.,* 2013).

Ten apparently healthy dogs with no skin affection were included irrespective of age, sex and breed and were chosen randomly to act as control. Blood sample was taken into vial containing EDTA for estimation of blood parameters Haemoglobin (Hb), Total leucocyte count (TLC) using fully automatic Haematology analyser, Differential leucocyte count (DLC) was done using Leishman's stain as per the method suggested by Jain (1986). Another sample was taken without anti-coagulant for the estimation of biochemical parameters (total protein, albumin, globulin, A: G, total bilirubin and ALT) using fully automated chemistry analyzer, using reagent Kits.

The levels of IgE in serum of atopic dogs was estimated using Canine IgE ELISA kit.

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

Prevalence

The prevalence of atopic dermatitis in our study among various skin affections in dogs were recorded as 27.90% (52/186) and this was in agreement with Daigle *et al.* (2010) who documented that occurrence of canine atopic dermatitis may range from 3 to 30%, whereas Hillier (2002) reported that prevalence of atopic dermatitis is around 10 to 15% among canine population and 21.60% amongst dogs presenting with signs of skin diseases.

Atopic dermatitis was found to be highest during monsoon (32.53%) and least in winters (18.75%) (Table 1). This was similar to the reports by Chhabra *et al.* (2000) who found maximum cases of skin affections (77.90%) during the rainy season and found minimum infestation (28.20%) in the winter season. This might be because of hot and humid

Lesions/ signs	0	1	2	3	4	5
Pruritis	absence	mild	moderate	Severe	—	—
Erythema	absence	Presence of few red macules of low intensity	Presence of several red macules	Presence of several red macules over a wider area	Intense reddish color	Intense reddish color over a wider area
Alopecia	absence	Slight hairfall	Moderate hairfall with few patches	Moderate hairfall with several patches	Larger patches of alopecia	Patches of alopecia covering whole body

environmental conditions that favour the development of the parasites and the animals remain wet for long duration which further enhances the precipitation of these disorders (Dimri, 1998). Dimri and Sharma (2004) also reported that in hot and humid months of the year, skin disease in dogs were abundant.

Table 1: Season wise prevalence (percent) of atopic dermatitis in dogs

Season	Atopic (n=52)
Monsoon	27 (32.53%)
Autumn	5 (31.25%)
Winters	3 (18.75%)
Spring	4 (21.05%)
Summer	13 (25%)

Sex wise analysis revealed similar distribution among males (28.00%) and females (27.80%). Usually, there is no sex predilection for atopic dermatitis (Pocta and Svoboda, 2007). Though, higher incidence of the disease in male dogs (Nesbitt 1978) and higher incidence in female dogs (Scott, 1981; Nesbitt *et al.,* 1984) has been reported. Sex susceptibility should be analysed in light of observation that people in the region prefer male dogs over females.

Table 2: Age wise presentation of atopic dermatitis in dogs

Age	Atopic (n=52)
0-12 months	9 (17.30%)
1-3 years	24 (46.15%)
3-5 years	10 (19.23%)
> 5 years	9 (17.30%)

Atopic dermatitis was observed maximum in the age group of 1-3 years (46.10%) followed by 3-5 years (19.20%) (Table 2). Allergies tend to appear more in mature animals, probably because repeated exposure to antigen must occur and the immune response has to occur before clinical manifestations develop. Daigle *et al.* (2010) opined that canine atopic dermatitis is likely to be a lifelong condition that typically manifests itself before 3 years of age. Canine atopic dermatitis is usually diagnosed in patients from 6 months to 3 years of age (Saridomichelakis *et al.,* 1999), but its clinical signs were also observed in animals under 6 months and over 7 years of age.

Atopic dermatitis occurred mainly in Labrador and toy breeds (30.70%) followed by German Shepherds (11.50%) (Table 3). Other breeds affected were Golden Retriever, Bully, St. Bernard, Tibetan mastiff, Pit bull, Bull terrior and non-discript breeds. The findings of present study was in agreement with (Nagata, 2000) who also found German shepherd, Boxer, Dalmatian, Pug, Golden Retriever, Labrador, Lhasa Apso, Shih Tzu are genetically predisposed.

Table 3: Breed wise prevalence (percent) of atopic dermatitis

Breeds	Atopic
Labrador	16 (30.76%)
GS	6 (11.53%)
Toy breeds	16 (30.76%)
ND	3 (5.76%)
Bully	1 (1.92%)
Mastiff	1 (1.92%)
Golden Retriever	3 (5.76%)
Pit bull	1 (1.92%)
Bull terrior	2 (3.84%)
St. Bernard	3 (5.76%)
Total	**52**

*Toy breeds- Pomerarian, Spitz, Pug, Dashchund, Lhasa Apso

Clinical signs

Cases of atopic dermatitis showed itchy and red with bumps flaky circular lesions and hairloss. Pruritus, alopecia and erythema were the most common clinical signs in cases of atopic dermatitis (Table 4).

Table 4: Lesions recorded in canine atopic dermatitis

Lesions	No. of dogs=52
Pruritis	52 (100%)
Erythema	43 (82.69%)
Alopecia	39 (75%)
Hyperpigmentation	19 (36.53%)
Papules, scales, crust	13 (25%)
Lichenification	11 (21.15%)

Excoriation	10 (19.6%)

Favrot *et al.* (2010) also recorded that 61.00% atopic dermatitis affected dog showed pruritus which is the most pathognomic sign of atopic dermatitis. Face rubbing and foot licking were predominantly observed. The significant lesions noticed in the present study were in agreement with Olivry *et al.* (2007). Some cases showed seasonal variation (25.00%) while most of the cases revealed non seasonal dermatitis (75.00%). The affected dogs lived indoors in maximum number of cases and there was no history of recent change of diet and unresponsive pruritus in all the cases of atopy. In 61.53% (32) cases, there was proliferation of staphylococci leading to superficial pyoderma. In addition, malassezia was also found in 46.15% of the cases. Lesions were more frequently seen at groin, abdomen, neck, axilla, face and less commonly at limbs and tail (Table 5) (Fig. 1, 2, 3). Chronic skin changes such as seborrhea, hairloss, hyperpigmentation and lichenification were recorded. These findings were in agreement with Andrew (2002) who reported that perioccular, muzzle and chin (face), medial aspect of ear pinna, ventrum, neck, axilla, abdomen, tarsal or carpal area and digits were specific sites where atopic lesions were distributed.

Table 5: Affected sites observed in atopic dermatitis affected dogs

Sites	No. of dogs affected (n=52)
Groin	46 (88.4%)
Abdomen	41 (78.8%)
Neck	40 (76.9%)
Perioccular	39 (75%)
Axilla	37 (71.1%)
Muzzle	36 (69.2%)
Paws	36 (69.2%)
Ear pinna	35 (67.3%)
Limbs	25 (48.07%)
Tail	4 (7.6%)

Diagnosis

Out of total 186 dogs, 52 dogs were diagnosed as atopic on the basis of exclusion criteria, serum IgE levels, interpretation of detailed history and characteristic clinical findings along with Favrot's criteria. Use of any one of these approaches in isolation can result in misdiagnosis, so it is important not to rely on any of them as a sole diagnostic principle. In our study 32/52 (61.53%) dogs fulfilled five (out of eight) diagnostic criteria. All the dogs (100%) did not fit into this criteria, it might be because when a patient is presented at an older age and the history of onset of disorders reported by the owner is not exact, the choice for the remaining criteria is lower. Further, administration of corticoids does not always result in control of pruritus; numerous patients suffer from other types of hypersensitivity. Involvement of the dorsolumbar region also cannot be employed to differentiate atopic dermatitis from flea allergy dermatitis (Griffin and DeBoer, 2001). Overall, it is possible to use the clinical criteria by Favrot *et al.* (2010) to be used as an auxiliary means for the clinical picture of atopic dermatitis.

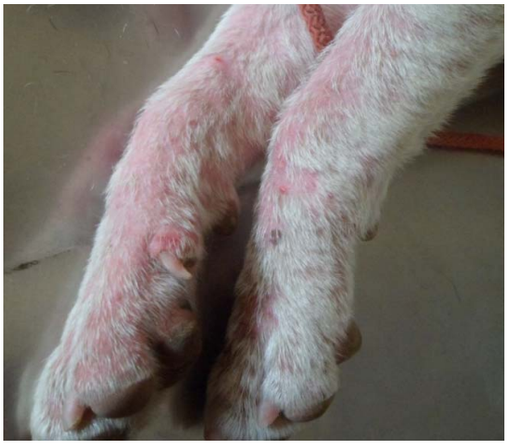

Fig. 1: Erythema of forelimbs in a dog with atopic dermatitis

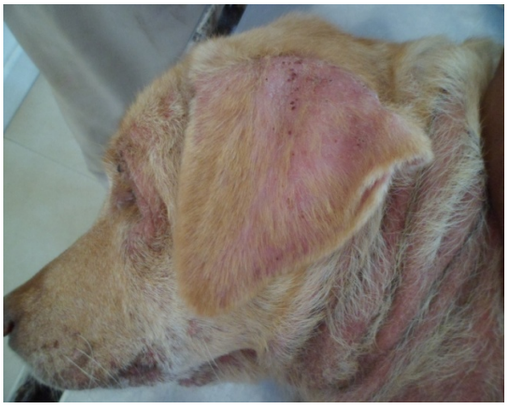

Fig. 2 : Atopic dermatitis in a dog showing erythema and

thickening of skin

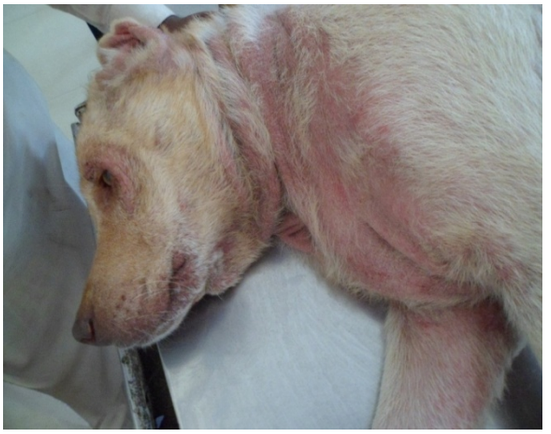

Fig. 3: Alopecia and erythema on face, ears, neck, axilla, limbs in an atopic dog

The serological estimation of IgE through ELISA revealed 33/52 (63.46%) AD cases had higher serum IgE levels and 19/52 (36.54%) had lower levels of IgE when compared to healthy dogs. Elevated levels of IgE were in agreement with (Scott *et al.,* 2001, Walaa *et al.,* 2008). Some studies suggest that atopic dermatitis is not always IgE mediated (DeBoer, 2004, Olivry *et al.,* 2010). Nagata (2000) opined that there is no single distinguishing feature or a simple, definitive, diagnostic laboratory test to diagnose allergic dermatitis. Many normal and atopic dogs exhibit positive reactions with allergy test, thereby markedly decreasing the tests' specificity for the diagnosis of AD. Using a serologic test or intradermal tests a primary criterion for diagnosing AD will, therefore lead to misdiagnosis.

Haematological findings

The haemoglobin concentration did not changed significantly in affected dogs (12.9±0.32) as compared to healthy (13.9±0.33) dogs (Table 6) which is similar to the findings of Sharma *et al.* (2015b) who observed no significant change in haemoglobin levels in healthy and allergic dogs. Leukocytosis was observed in atopic dogs (16424.9±1013.3) when compared to healthy ones (8803.0±713.6). Leukocytosis could be due to cellular and hormonal immune response in atopic 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). Neutrophilia was also observed in atopic dermatitis affected dogs (76.8±1.90) as compared to healthy (64.6±2.35). Neutrophilia observed in the 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). Lymphocytes did not show any significant changes (17.6±1.54) as compared with healthy ones (17.6±1.54). However, Latimer (1995) observed lymphocytosis in allergic dermatitis. Eosinophilia was also observed in atopic dogs (5.1±0.77) as compared to healthy dogs (0.6±0.31). It might have occurred due to hypersensitivity reaction because of raised histamine concentration which causes release of eosinophils in the blood circulation. Wuersch *et al.* (2006) also found that atopic dogs expressed high level of eosinophils because of the mast cells stimulation via IgE receptors whereas some researchers like Wilkie *et al.* (1990) and Collie *et al.* (1997) reported that eosinophilia may not always be related to allergic diseases.

Table 6: Hemato-biochemical (Mean±SE) of healthy and atopic dogs

Parameters		Control (n=10)	Atopic (n=52)
Hb (g/dl)		13.9±0.33	12.9±0.32
TLC(10^3/cumm)		8803.0±713.6	16424.9±1013.3*
DLC	N (%)	64.6±2.35	76.8±1.90*
	L (%)	20.3±2.50	17.6±1.54
	E (%)	0.6±0.31	5.1±0.77*
Total protein (g/l)		6.7±0.11	5.8±0.14*
Albumin (g/l)		3.3±0.11	2.8±0.09
Globulin (g/l)		3.5±0.12	3.1±0.14
A:G		0.9±0.15	1.0± 0.28

*: significant ($p<0.05$)

Biochemical findings

Serum total protein values significantly decreased in atopic dogs (5.8±0.14) as compared to healthy (6.7±0.11) (Table 6) in agreement with that of Aujla (1993) and Ramakrishnan *et al.* (1972). However, Sharma and Gupta (2005) observed no change in protein value in dermatitis.

Albumin and globulin values were mildly decreased in atopic dogs as compared to healthy ones (Table 6). The low serum albumin value may be due to impaired nutrition in severe dermatitis due to general weakness and more utilization of dietary protein in the globulin synthesis. A: G ratio was slightly increased in atopic dogs when compared to healthy dogs which could usually alter by a decrease in albumin and/or an increase in globulins. Ramakrishnan *et al.* (1972) also observed an increase in A: G ratio.

Serological findings

The serological estimation of IgE through ELISA was done for the diagnosis of atopic dermatitis in dogs. It was found that the IgE levels in the sera of dogs was higher (271.41±55.5) as compared to normal dogs (40.47±6.9) (Table 7).

Table 7: Serological estimation of IgE (Mean±SE) in serum of healthy and atopic dogs

Parameter	Control (n=10)	Atopic (n=52)
IgE (µg/ml)	40.47±6.9	271.41± 55.5*

*significant ($p<0.05$)

The high production of IgE is 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.

REFERENCES

Aujla, R.S. 1993. 'Etiopathology of cutaneous affection in canine'. M.V.Sc. Thesis, Punjab Agricultural University, Ludhiana, India.

Chhabra, S., Khahra, S.S. and Nauriyal, D.C. 2000. Effect of treatment on haemato biochemical indices in canine acariosis. *J. Vet. Parasitol.,* **14(2)**: 147-149.

Collie, D.S., DeBoer, D.J., Muggenberg, B.A. and Bice, D.E. 1997. Evaluation of association of blood and bronchoalveolar eosinophil numbers and serum total IgE concentration with the expression of non specific airway reactivity in dogs. *Am. J. Vet. Res.,* **58**: 34- 39.

Daigle, J., Moussy, A., Mansfield, C.D., Hermine, O. 2010. Masitinib for the treatment of canine atopic dermatitis: a pilot study. *Vet. Res. Commun.,* **34**: 51-63.

DeBoer, D.J. 2004. Canine atopic dermatitis: New targets, new therapies. *J. Nutr.,* **134** (8suppl): 2056S-2061S.

Dimri, U. 1998. 'Clinicotherapeutic studies on skin diseases in dogs, sheep and goats'. Ph.D. Thesis, Deemed University, Indian Veterinary Research Institute, Izatnagar, India.

Dimri, U. and Sharma, M.C. 2004. Effects of Sarcoptic Mange and its Control with Oil of Cedrusdeodara, Pongamiaglabra, Jatrophacurcas and Benzyl Benzoate, both with and without Ascorbic Acid on Growing Sheep: Epidemiology; Assessment of Clinical, Haematological, Cell-Mediated Humoral Immune Responses and Pathology. *J. Vet. Med.,* **51 (2)**: 71-78.

Favrot, C., Steffan, J., Seewald, W. and Picco, F. 2010. A prospective study on the clinical features of chronic atopic dermatitis and its diagnosis. *Vet. Dermatol.,* **21**: 23-31.

Fontaine, J and Olivry, T. 2001. Treatment of canine atopic dermatitis with cyclosporine: a pilot clinical study. *Vet. Rec.,* **148**: 662-663.

Griffin, C.E. and Deboer, D.J. 2001: The ACVD task force on canine atopic dermatitis (XIV): clinical manisfestations of canine atopic dermatitis. *Vet. Immunol Immunopathol.,* **81**: 255-269.

Gupta, N. and Prasad, B. 2001.Clinical diagnosis and therapeutic management of Acariasis in dogs. *Indian J. Vet . Med.,* **21 (2):** 73-75.

Halliwell, R. 2006. Revised nomenclature for veterinary allergy. *Vet. Immunol Immunopathol.,* **114(3-4):** 207-208.

Hill, P.B. and DeBoer, D.J. 2001. The ACVD task force on canine atopic dermatitis (iv): environmental allergens. *Vet. Immunol. Immunopathol.,* **81:** 169-186.

Hillier, A. 2002. Definitively diagnostic atopic dermatitis in dogs. *Vet. Dermatol.,* **22**: 198-208.

Jain, N.C. 1986. *Schalm's Veterinary haematology*. 4th Ed., Lea and Febiger comp., Philadelphia, pp. 263-417.

Latimer, K.S. 1995. Leukocytes in health and disease. In: *Textbook of Veterinary Medicine. Diseases of Dog and Cat.* Ettinger S J and Feldman E C (Eds.). W.B. Saunders Comp., Philadelphia. pp. 1057-1063.

Nagata, M. 2000. Diagnosis of atopic dermatitis in dogs. *Waltham Focus.,* **10**: 4-9.

Nambi, A.P. and Kavitha, S. 2013. Canine Atopic Dermatitis. *Intas Polivet.,* **14(2):** 236-240.

Nesbitt, G.H. 1978. Canine allergic inhalant dermatitis: a review of 230 cases. *J. Am. Vet. Med. Assoc.,* **172**: 55-60.

Olivry, T., DeBoer, D.J. and Favrot, C. 2010. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. *Vet.*

Dermatol., **21(3):** 233-248.

Olivry, T., Marsella, R., Iwasaki, T. and Mueller, R. 2007. The international task force on canine atopic dermatitis validation of CADESI-03, a severity scale for clinical trials enrolling dogs with atopic dermatitis. *Vet. Dermatol*., **18**: 78-86.

Pocta, S. and Svoboda, M. 2007. Approach to the diagnostics of atopic dermatitis in dogs in conditions of clinical practice. *Acta Vet. Brno,* **76**: 461-468.

Puigdemont, A., Brazís, P., Ordeix, L., Dalmau, A., Fuertes, E., Olivar, A., Pérez, C. and Ravera, I. 2013. Efficacy of a new topical cyclosporine A formulation in the treatment of atopic dermatitis in dogs. *Vet. J.,* **197**: 280-285.

Ramakrishan, R., Sundaraj, A., Damodaran, S. and Chanderasekaran, K.P. 1972. Hemogram and serum proteinogram in some canine disease. *Cheiron.,* **1(1)**: 11-20.

Saridomichelakis, M.N., Koutinas, A.F., Gioulekas, D. and Leontidis, L. 1999. Canine atopic dermatitis in Greece: clinical observations and the prevalence of positive intradermal test reactions in 91 spontaneous cases. *Vet. Immunol. Immunopathol.,* **69**: 61-73.

Schalm, O.W. 1963. Interpretation of leucocytic response in dogs. *J. Am. Vet. Med. Assoc.,* **142**: 147-152.

Scott, D.W., Miller, W.H. and Griffin, C.E. 2001. Skin immune system and allergic skin disease. In: *Muller and kirk's Small Animal Dermatology.* 6thEd., WB Saunders comp., Philadelphia, pp. 543-666.

Sharma, J. and Gupta, G.C. 2005. Serum protein profiles in naturally occurring dermatological disorders in dogs. *Indian J. Vet. Med.,* **25(1)**: 33-34.

Sharma, R., Hussain, K., Chhibber, S., Kumar, M. and Sharma, N. 2015a. Allergic Dermatitis Occurrence Pattern in Canine of Jammu Region*. Indian J. Anim. Res*., **5(3):** 533-537.

Sharma, R., Hussain, K., Chhibber, S., Kumar, M. and Singh, R. 2015b. Clinico-haematological and biochemical studies in allergic dermatitis in dogs. *Indian J. Canine Pract.,* **7(2)**: 124-129.

Snedecor, G.W. and Cochran, W.G. 1994. *Statistical Methods*, 8thEd., Oxford and IBH Publications, New Delhi.

Walaa, I.M., Asmaa, O.A. and Elsayed, R.F. 2008. Clinical and laboratory studies on canine atopic dermatitis in dogs. *SCVMJ,* **13(1)**: 191-126.

Wilkie, J.S., Yager, J.A., Eyre, P. and Parker, W.M. 1990. Morphometric analysis of the skin of dogs with atopic dermatitis and correlations with cutaneous and plasma histamine and total serum IgE. *Vet. Pathol.,* **27**: 179-186.

Willemse, T. 1986. Atopic skin disease: a review and reconsideration of diagnostic criteria. *J. Small. Anim. Pract.,* **27**: 771-778.

Willemse, T. 1988. Atopic dermatitis in the dog: new diagnostic criteria. *Tijdschr. Diergeneeskd.,* **113**: 74-79.

Wuersch, K., Brachelente, C., Doh-err, M., Reist, M., Sattler, D., For-ster, D., Bertoni, G., Peel, J, E. and Welle, M. 2006. Immune dysregulation in flea allergy dermatitis-A model for the immunopathogenesis of allergic dermatitis. *Vet. Immunol. Immunopathol.,* **110**: 311-323.