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Clinical, Hematological and Some Biochemical Changes In Dogs Infected With Canine Distemper

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Abstract
This works was conducted to determine the incidence of canine distemper disease (CDD) in dogs in Mosul city, Iraq using sandwich ELISA test and to evaluate the clinical, haematological and some biochemical parameters in dogs. A total 92 blood samples were collected from dogs (23 Pet dogs and 69 stray dogs), which include 10 clinically healthy dogs used as control group. Each dog was carful clinically exanimated. The overall sero-incidence of CDV antigen was 18/92 (19.5%), comprising 1/23(4.34%) in pet dogs and 17/69 (24.6%) stray dogs. The incidence of CDV was significantly higher in stray dogs compared to pet dogs (P< 0.05). Infected dogs were suffering from loss of appetite, lethargy, oculonasal discharges, coughing, vomiting, diarrhea, dehydration, thickening of the foot pad and around the nose and nervous signs with different frequency and percentage. Other exhibited in infected dogs were significantly increase in the body temperature, respiratory and heart rates compared to control group (P<0.05). The haemogram of the infected dogs revealed that significantly decrease in TEC, Hb, PCV, Thrombocytes, TLC, lymphocytopenia, MCV, MCH and MCHC, reflecting a microcytic hypochromic type of anemia, along with significant increase in the ESR compared to control group (P<0.05). Serum biochemical profile of the infected dogs showed significant increase in ALT, AST, ALP, BUN, TB and creatinine, along with significantly decrease in the TP, compared to control group (P<0.05). This study indicate that CDV is widespread in dogs in Mosul city with significant clinico-pathological parameters alteration in infected dogs.

Key words: *Canine distemper virus, Sandwich ELISA test, Clinical signs, Hematology, Biochemical.*

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I. Introduction

In Iraq, canine proprietorship is an expanding for many purposes such as hunter dogs, police dogs, pet dogs, guard dogs and assistant dogs, that needs special approach since it lack necessary data such as prevalence of various diseases and other essential information in this regard (Tamimi, 2017). Canine distemper disease (CDD) is a sever contagious and often fatal infectious disease affects Canidae (Dogs, Foxes, Wolves, Raccoon) and a broad range of wild and aquatic animals (Martinez-Gutierrez and Ruiz-Saenz, 2016; Loots et al., 2017). It is distribution over all world with highly morbidity/mortality in spite of vaccinated animals and has no specific treatment (Feng *et al.,* 2016;Saltik and Kale 2020). The disease caused by Canine distemper virus (CDV) is belonging to the group of single-stranded RNA virus of the family Paramyxoviridae and Morbillivirus genus (ICTV, 2014). The virus can be transmitted mainly by inhalation through air droplets contaminated with the secretions of infected dogs, through direct contact with the secretions of infected dogs includes oronasal secretions, blood and urine, feces, skin and through pots fomites contaminated with these secretions (Di Sabatino *et al.*, 2014; Megid *et al.,* 2014). Furthermore, transplacental transmission (Sykes, 2013). The CDD infects puppies with highly mortality rate reach to 80% and unvaccinated adult dogs with 50% mortality rate, that act as the main reservoir host for the virus (Gray *et al.,* 2012; Wyllie *et al.,* 2016). Canine distemper virus incubation period ranges between 1-3 weeks, after which the animals affected by the disease show various or different clinical signs, depending on the stage of the disease (Amude *et al.,* 2006). The clinical manifestation in the infected dogs with canine distemper includes; respiratory signs (mucopurulent oculo-nasal discharge, coughing, sneezing, dyspnea and respiratory distress), and/ or gastrointestinal sings (anorexia, increase salivation, tooth enamel hypoplasia, vomiting, diarrhea and dehydration), Ocular signs (eyelid swelling, congestion in the conjunctiva and ocular purulent secretions), with or without neurological signs (seizures, hypersensitivity, chewing-gum movement, paddling, ataxia, chorea, muscle termers, cycling movement, and plegia or paresis), cutaneous signs (hyperkeratosis of the nostril and footpad and red rashes) and

immunosuppression also can be seen (Bittegeko *et al.*, 1995; Carvalho *et al.*, 2012; Elia *et al.*, 2015; Buragohain *et al.*, 2017; Amude *et al.*, 2018; Saltik and Kale, 2020). Furthermore, canine naturally infected with CDV have alteration of hematological and serum chemistry parameters (Buragohain et al. 2017; Yama *et al.*, 2020).Sandwich-ELISA test is a specific and sensitive assay for detection of different CDV antigen that could be suitable for high-throughput testing applications (Abbexa, 2020 ; Zhang *et al.*, 2020). No studies of CDD in Mosul city, Iraq and to the best knowledge of this researcher, no information on incidence, hematology, and biochemical parameters. Therefore, this study has been designed to determine the incidence of CDD and to determine the clinical, hematological and some biochemical parameters alterations in dogs.

II. Material And Methods

Ethical approval

The study has been approved by the Department of Internal and Preventive Medicine, College of Veterinary Medicine, University of Mosul, Mosul, Iraq. In addition, the blood samples were obtained in accordance with the recommended "standard sample collection procedure" which ensured that animals were not subjected to any stress or harmed in any way.

Animals and samples collection

The study was conducted on carful clinically exanimated of 92 dogs (69 stray dogs and 23 Pet dogs) comprising 10 clinically healthy dogs used as control group, from both sexes and different breeds (Local ,German and Husky) with ages ranging between (2 months – 1.5 years), were brought to the veterinary teaching hospital, some private veterinary clinics and from different villages of the Mosul city, Iraq. Each dog was laboratory examined to ensure that it is free from internal and external parasites according to Weiss & Wardrop, (2010). From September, 2020 to March, 2021, 92 blood samples were withdrawn from each dog via the cephalic vein using 5ml syringe, the blood placed in to two tubes, one with ethylenediaminetetraacetic acid (EDTA) anticoagulant for complete blood counts. A second tube without anticoagulant for separating the serum using a centrifuge at a speed of 2500 rpm for 10 minutes, then stored -20 m ° until used for sandwich ELISA test for detection CDV antigen.

Sandwich enzyme linked immunosorbent assay

This assay was used as conforming test to detect the antigen of canine distemper virus in 92 blood serum samples using the canine distemper virus ELISA test kit provided by the American company (Abbexa LLc, USA), according to manufacture instructions.

Hematological analysis

Blood samples were tested for hematological analysis using hematology analyzer (Genex-California.USA) to get the total erythrocyte count (TECs), haemoglobin concentration (Hb), packed cell volume (PCV), platelets counts (PLT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and total leukocytes count (TLCs). Thick blood smears were prepared and stained with MGG-Quick stain (Bio-Optic, Italy) were used for differential leukocytes count(DLC). In addition, Westergren method used for estimation of erythrocyte sedimentation rate (ESR) (Weiss and Wardrop, 2010).

Biochemical analysis

Blood serum samples were tested for some biochemical analysis using spectrophotometer (Cecil, England) for estimation of alanine amino transferase (ALT) with IU/L, aspartate amino transferase (ALT) with IU/L, alkaline phosphatase (ALP) with IU/L, total bilirubin (TB) with mg/100ml, total protein (TP) with g/100ml using available kits, blood urea nitrogen (BUN) with mg/100ml, and creatinine with mg/100ml (In this study all biochemical parameter were estimated using available kits provided from (Randox, British), except total bilirubin (TB) estimated using available kits provided from (Biomerex, France).

Statistical analysis

The results of this study were analyzed using the statistical program IBM-SPSS version 22. two-sides chi-square test, and Fischer's test were used evaluate the difference in the incidence between pet and stray dogs base on sandwich ELISA test. Furthermore, independent sample *t*-tests was used to determine the significance of variations between diseased and healthy cats in haematological and some biochemical parameters. All the significant differences were determined at ($P<0.05$).

III. Results

In this study the results of examination of 92 serum samples of dogs revealed that the overall incidence of canine distemper virus (CDV) in dogs in Mosul city, Iraq was 18/92 (19.5%) , in stray dogs was 17/69 (24.6%) and in pet dogs was 1/23 (4.34%) based on sandwich ELISA test, these indicates that the incidence of CDV in stray dogs was significantly higher than in pet dogs (P <0.05) (Table 1). Carful clinical examination of dogs indicates that the dogs infected with canine distemper disease (CDD) were suffering from loss of appetite, fever, lethargy, oculo-nasal discharges, coughing, vomiting, diarrhea, dehydration, thickening of the foot pad and around the nose, and nervous signs (Circling movement, head tilt, muscle twitches, chewing-gum movement and paralysis) with different frequency and percentage (Figure 1,2). Other symptoms in infected dogs were significantly increase in the body temperature (39.9 C°), respiratory rate (48.6/min)and heart rate (108.4/min) compared to control group (P<0.05) (Table 3).

In the current study, blood hematologoical analysis of the infected dogs revealed that significantly decrease in TEC, Hb, PCV, PLT (Thrombocytopenia), TLC, lymphocytopenia, MCV, MCH and MCHC, reflecting a microcytic hypochromic type of anemia, along with significant increase in the ESR compared to control group (P<0.05) (Table 4). Moreover, serum biochemical profile of the infected dogs showed significant increase in ALT, AST, ALP, BUN, TB and creatinine along with significantly decrease in the TP , compared to control group (P<0.05) (Table 5).

Table 1: Incidence of canine distemper virus in stray and pet dogs using sandwich ELISA test.

Type of dogs	No. of samples tested	Sandwich ELISA test
		No. of positive samples (%)
Stray dogs	69	17 (24.6)[a]
Pet dogs	23	1 (4.34)[b]
Overall	92	18 (19.5%)

The different superscript letters (a or b), indicate that the values were significantly different (P < 0.05).

Figure 1: Some clinical signs shown on dogs infected with canine distemper virus.

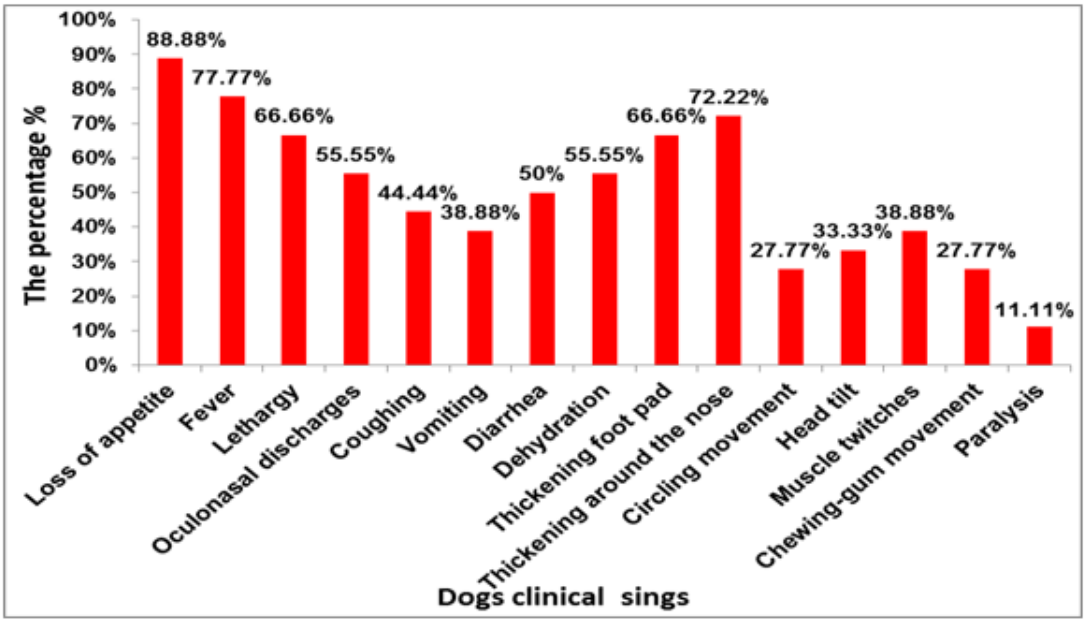

Figure 2: The percentage of clinical signs on dogs infected with canine distemper virus (18 Cases).

Table 3: Clinical parameters of dogs infected with canine distemper virus and healthy group. Data are presented as mean ± standard error of mean

Parameters	Control group (n=10)	Infected dogs (n=18)
Body temperature, °C	38.1 ± 0.43	39.9 ± 0.58*
Respiratory rate, 1 min	29.78 ± 4.36	48.6 ± 6.56*
Heart rate, 1 min	77.92 ± 5.43	108.4 ± 11.14*

* P<0.05 between infected dogs and control group.

Table 4: Blood parameters in dogs infected with canine distemper virus and healthy group .Data are presented as mean ± standard error of mean.

Parameters	Control group (n=10)	Infected dogs (n=18)
TEC, $\times 10^{12}$/L	6.38 ± 0.17	4.95 ± 1.22*
Hb, g/ dL	12.75 ± 0.52	10.51 ± 1.34 *
PCV, %	39.14 ± 1.23	31.42 ± 2.57*
MCV,fl	58.17 ± 0.51	53.97 ± 1.72 *
MCH, pg	23.22 ± 1.11	19.33 ± 1.15*
MCHC, g/dl	32.11 ± 1.74	29.36 ± 1.74*
ESR, mm/hour	0.12 ±0.06	0.61 ± 0.30*
PLT, 10^9/L	320.09 ± 26.77	228.00 ± 36.31*
TLC, $x10^9$/L	12.04 ± 1.61	9.70 ± 1.83*
Lymphocytes, % Absolute	24.36 ± 9.78 2932 ± 978.6	15.50 ± 2.75* 1503 ± 266.6
Neutrophils, % Absolute	59.64 ± 3.49 7180 ± 420.1	61.17 ± 4.23 5933 ± 410.3
Monocytes, % Absolute	12.93 ± 2.31 155 ± 27.7	12.37 ± 1.22 119 ± 11.7
Eosinophils, % Absolute	3.00 ± 1.26 361 ± 15.2	2.63 ± 0.80 255 ± 7.75

Basophils, % Absolute	0.30 ± 0.16 36 ± 1.92	0.38 ± 0.05 36 ± 4.73

* P<0.05 between infected dogs and control group.

Table 5: Serum biochemistry parameters in dogs infected with canine distemper virus and healthy group .Data are presented as mean ± standard error of mean.

Parameters	Control group (n=10)	infected cats (n=18)
AST, U/L	25.88 ± 5.70	57.18± 9.8*
ALT, U/L	29.12 ± 7.63	62.25 ± 11.22*
ALK, U/L	108.44± 12.11	217.81± 16.22*
TB, mg/100ml	0.12± 0.11	0.62 ± 0.12*
Total protein g /dl	5.21± 1.43	2.61 ± 1.23*
BUN mg/dl	18.26± 6.28	29.16 ± 5.44*
Creatinine mg/dl	0.54± 0.21	1.42 ± 0.23*

* P<0.05 between infected dogs and control group.

IV. Discussion

This is the first report of CDD in stray and pet dogs in Mosul city, Iraq. In this study the overall incidence of canine distemper virus (CDV) in dogs in Mosul city, Iraq was 18/92 (19.5%) based on sandwich ELISA test. This result is higher in comparison to prevalence of CDV in other countries such as: in Iran was 17.52% using Indirect immunofluorescent assay (IFA) (Avizeh *et al.,* 2007), in Haa, Western Bhutan was 11.3%, using sandwich enzyme-linked immune-sorbent assay (ELISA) test (Dorji *et al.,* 2020) and in Mizoram, India was as1.11% using the antigen rapid CD virus Ag test kit (Yama *et al.,* 2020). While, our result is lower prevalence to that reported in other countries such as: in Turkey, 94% IgG and 58% IgM positive samples were detected by the CDV-specific indirect ELISA in the 50 serum samples (Saltik & Kale, 2020), in Thimphu capital city of Bhutan was 49.7% using sandwich enzyme-linked immune-sorbent assay (ELISA) test (BBS, 2019), and in Brazil, the detection rate of CDV in urine samples was 36.6%, 100% in symptomatic dogs tested using RT-PCR and One-Step RT-qPCR (Silva *et al.,* 2014; Tozato *et al.,* 2016) respectively**.** The prevalence of CDV in different studies and different areas is varies, may be related to the percentage of specificity of diagnostic methods, stage of CD present and the vaccination status of dogs (Nova *et al.,* 2018). This study indicates that the incidence of CDV in stray dogs was significantly higher than in pet dogs. This finding agrees with the results of Gencay *et al.* (2004) and Swapna *et al.* (2018) They mention that higher prevalence of CDV in stray dogs which were 9.03% and 4% respectively. In addition, Gog *et al.*(2002) and Acosta-Jamett *et al.* (2011) revealed that a maintained canine population management and pet possession are the only arrangements to reduce canine population, which would, in turn, reduce canine-wildlife interactions and outcomes pathogen spreading. On the other hand, Dorji et al. (2020) and Saltik and Kale, (2020) mentioned that no significant difference in the prevalence of CDV between stray and pet dogs. In particular, vaccination programmes for pet dogs are more used in private veterinary clinics. Nevertheless, since no vaccination programme is applied to stray dogs, all the vaccinated or unvaccinated dogs are at risk of the disease (Lorusso and Savini, 2014). Sandwich enzyme linked immunosorbent assay (Sandwich-ELISA) was used in this study to detect the antigen of canine distemper virus. This test is sensitive, specific, and simplify assay with good reliability for detection of CDV antigen that could be suitable for high-throughput testing applications (Abbexa, 2020 ; Zhang *et al.,* 2020).

This study revealed that infected dogs with CDD showed loss of appetite, lethargy, eye and nasal discharges, coughing, vomiting, diarrhea, dehydration, thickening of the foot pad and around the nose and nervous signs. In addition, a significantly increase in the body temperature (39.9 C°), respiratory rate (48.6/min) and heart rate (108.4/min) compared to control group. these signs and symptoms were agreements with those reported by Willi *et al.* (2015); Buragohain *et al.* (2017); Amude *et al.* (2018); Saltik and Kale, (2020). The CDV infects various body systems including lymphatic, respiratory, digestive, urinary, skeletal, cutaneous, and central nervous systems (Lempp *et al.,* 2014). Canine distemper virus infections in dogs causes immunosuppression which favor for secondary bacterial infections that cause respiratory and gastrointestinal symptoms such as: diarrhea and vomiting (Beineke *et al.,* 2009; da Fontoura Budaszewski and Von Messling, 2016; Saltik and Kale, 2020). The thickening (hyperkeratosis) of the foot pad and around the nose were most dominantly signs reported in this study. Previous studies were reported similar finding (Schobesberger *et al.,* 2005; Elia *et al.,* 2015). The neurological signs in infected dogs were also described by Pan *et al.* (2013) and Galan *et al.* (2014) who mention that CDV cause damage of grey and white matter of central nervous system which probably cause nervous sings in infected dogs. In addition, dogs showed plegia and paralysis might be

have distemper leukoencephalitis and/or encephalomyelitis (Amude *et al.,* 2018; Ruiz-Saenz *et al.,* 2019).

In the current study, hematologoical analysis revealed that significantly decrease in TEC, Hb PCV and PLT values of dogs infected with CDV compared to control group. This finding indicate that CDV causing anemia in infected dogs which resulting from effect on hematopoietic system (Buragohain *et al.,* 2017). Furthermore, Bohn, (2013) and Carter, (2018) mentioned that the persistence of the CDV in the bone morrow can cause erythrocyte hypoplasia and bone marrow depletion and/or suppression which effect on hematopoietic precursors resulting decrease production of these values. Canine distemper infection cause release of interleukin-6 lead to iron deficiency with piokilocytosis, schistocytes, hypochromasia, keratocytes, microcytes and thus iron not accessible to create reticulocytes (Gordon *et al.,* 1992; Bohn, 2013).

A significantly decrease in MCH and MCHC values, reflecting a microcytic hypochromic type of anemia in dogs infected with CDV. Same results were reported by Headly and Sukura, (2009) and Buragohain *et al.* (2017). In present study leukopenia and lymphocytopenia in dogs infected with CDV. This is in agreement with Ezeibe and Udegbunam, (2008); Salem, (2014) and Yama *et al.* (2020). The main reason for decrease in TLC and lymphocytes is apoptosis in these cells induced by distemper virus (Okada *et al.,* 2000). In addition, spreading of the virus cause loss of B and T cells (Williams, 2001). On the other hand, Buragohain *et al.* (2017) Find that TLC and lymphocyte counts were within normal range. In this study, The percentages and absolute numbers of neutrophils, monocytes, eosinophils and basophils were found within normal ranges in infected dogs. However, other studies showed significant decrease in monocytes count in dogs with CD (Beineke, 2015), and significant increase in granulocytes in infected dogs, this probably due to secondary bacterial infection and inflammatory reaction (Berghoff and Steiner, 2011; Yama *et al.,* 2020). Our results showed significant increase in the ESR values in the dogs with CDV. There is a correlation between the ESR value and intensity of anemia due to infections (Jain, 2000).

Moreover, in this study, serum biochemical profile of the infected dogs with CDV showed significant increase in ALT, AST and ALP levels in serum. These findings were in agreement with Apple *et al.* (1994); Buragohain *et al.* (2017) and Willi *et al.* (2015). Increase in alkaline phosphatase might be due to gastrointestinal disorder resulting from CDV (Benjamin, 2007 ; Yama *et al.,* 2020). An observed significant increase in BUN, TB, and creatinine, along with significantly decrease in the TP in infected dogs in compare with control group. However, other workers found that the levels of TB, creatinine and TP were within normal range, with significant increase in BUN in dogs with CD (Sykes, 2013; Salem, 2014 and Willi *et al.,* 2015). An increase in BUN and creatinine levels are probably due to dehydration (Barsanti *et al.,* 2004; von Dehn, 2014).

V. Conclusion

Our study indicates that CDD was widely distributed among stray and pet dogs, with significantly higher in stray dogs in Mosul city, Iraq. Also, CD infection in dogs was showed different clinical manifestations with significant alteration in hematological and biochemical parameters.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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