Clinical and haemato-biochemical alterations with acute phase response in canine parvoviral enteritis

Ibrahim Abdullaziz, Mahmoud Aly, Ibrahim ElShahawy

1Department of Animal Medicine, Faculty of Veterinary Medicine, Alexandria University, Egypt.
2Department of Medicine and infectious diseases, faculty of veterinary medicine, university of sadat city

ABSTRACT

Canine parvoviral enteritis (CPV) is one of the most contagious fatal viral diseases in young puppies with subsequent alterations in homeostasis; This study was conducted on a total number of 35 puppies of different breeds, with age range of 2-6 months old with signs compatible with canine parvovirus enteritis. Another apparently healthy five puppies within similar age range were enrolled as healthy control group. Up on admission, clinical signs were recorded and rapid in-clinic IC test kit for detection of CPV Ag in feces. Blood samples were used to determine haemato-biochemical alterations along with Acute phase response values. Vomiting and foul-smelling bloody diarrhea with marked dehydration were the main recorded clinical signs. Hemogram of CPV infected dogs, revealed the presence of microcytic hypochromic anemia, significant leukopenia with marked lymphopenia and neutropenia. The total serum proteins, albumin, total globulins, sodium, potassium, chloride, levels were significantly decreased in CPV infected group than its level in healthy control dogs. On contrary the mean values of, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN) and creatinine were significantly increased in diseased dogs. Results of acute phase biomarkers revealed Significant increase in serum amyloid A (SAA), haptoglobin (Hp) and C-reactive protein (CRP) with significant reduction in mean values of serum albumin in diseased puppies. Based on obtained results, CPV enteritis has negative impact on haemato-biochemical biomarkers and strong expression of acute phase reaction in diseased dogs.

Keywords: Clinical, haemato-biochemical, Parvo, Dogs .

1. Introduction

Canine parvovirus enteritis is a highly contagious fatal viral disease of dogs caused by parvovirus type -2, which has a great affinity to invade lymphoid and intestinal tissues, and it is transmitted via fecal-oral routes through direct or indirect contact between infected and susceptible dogs (Prittie, 2004). Acute parvoviral enteritis has been seen in dogs of all breeds, age, and sex, but puppies between 6 weeks and 6 months appear to be more susceptible (Gombak et al., 2017). Factors that predispose to parvoviral infection in puppies are lack of protective immunity, intestinal parasites and overcrowded, unsanitary and stressful environmental conditions (Khare et al., 2020). Fever, lethargy, vomiting, dehydration, and diarrhea which alternated from mucoid to hemorrhagic are the most common recorded clinical signs associated with CPV (Lamm and Rezabek, 2008; Goddard and Leisewitz, 2010).

Acute phase response (APR) is a state of early, defense systemic reaction of the body modulated by trauma, neoplastic growth, bacterial, parasitic, and viral infection, burns, surgery and immunological disorders (Petersen et al., 2004). The main function of APR is mainly to restore the homeostasis by isolating and destroying the harmful agent and to activate the repair process (Janeway et al., 2001). Acute phase proteins (APPs) is a large group of proteins synthesized mainly in liver and consider one of the most important metabolic alterations accompanying early acute stages of diseases; named acute phase response (APR) (Ceciliani et al., 2012). Nowadays, APPs are considered as a sensitive markers of inflammation and can be classified according to the magnitude of their increase into [positive APPs such as haptoglobin (Hp), C-reactive protein (CRP), α1-acid-glycoprotein and serum amyloid A] or decrease into (negative APPs such as albumin and transferrin) in serum concentrations within a few hours following infection (Murata et al., 2004; Gruys et al., 2005).

This study aimed to highlights the haemato-biochemical alterations associated with cases of canine parvovirus enteritis presented to small animal clinic, teaching hospital, Faculty of Veterinary Medicine, Alexandria University, Egypt with special focus on acute phase proteins [CRP, Hp, SAA and albumin] as a diagnostic indicator in CPV infected dogs..

*Corresponding author:
Email address: mahmoudaly@vet.usc.edu.eg

Departement of Medicine and infectious diseases, faculty of veterinary medicine, university of sadat city

2. Materials and Methods

2.1. Study design:
A total number of 35 puppies of different breeds, with age range of 2-6 months old were admitted to small animal clinic, teaching hospital, Faculty of Veterinary Medicine, Alexandria University in the period from January 2019 to June 2021, with signs compatible with canine parvovirus enteritis. Another apparently healthy five puppies within similar age range were enrolled as healthy control group. All dogs were clinically examined, and clinical signs were recorded at time of admission (Table 1, 2). Fecal samples from diseased dogs were collected for microscopic examination to ensure that dogs were free from parasitic infestation (Bellwood and Andrasik-Catton 2014). In-clinic rapid CPV Ag rapid kits were used on stool of suspected dogs (Quacking Biotech Co. Ltd. Shanghai, China) (Fig. 1).

Only dogs give positive results upon IC-test were enrolled in this study as diseased group (CPV infected dogs). Blood samples from all dogs were withdrawn and divided into 2 tubes; EDTA-containing tubes that was used for hematological analysis and plain tube was used for serum separation for further biochemical analysis.

2.2. Clinical examination:
Case history and clinical examination of all dogs under investigation was performed according to the method described by (Ettinger, 2010). Including temperature, pulse, respiration, mucous membrane evaluation and capillary refill time (CRT) (Table 1).

2.3. Sampling and Measurements:
Blood samples that were collected from cephalic vein of each dog are conducted for determination of: Red blood cell count (RBCC X10¹⁰/µl), hemoglobin concentration (Hb g/l), packed cell volume (PCV%), mean corpuscular volume (MCV fl), mean corpuscular hemoglobin (MCH pg), mean corpuscular hemoglobin concentration (MCHC g/dl), WBCs count (X10³/µl) and differential leucocytic count all were determined by using of fully automated veterinary hematology analyzer (Exigo, Boule medical AB., Sweden) in the central laboratory, Faculty of veterinary medicine, Alexandria University.

Determination of serum concentrations of Sodium, Potassium, Chloride, AST, ALT, Alkaline phosphatase (ALP), Total proteins and Albumin all were carried out by using commercial test kits supplied by (Bio-labo, France) while analysis of BUN (blood urea nitrogen) and creatinine were carried out by using commercial test kits supplied by (Ben-Biochemical Enterprise, Italy) all were analyzed following standard methods mentioned in the leaflet of the manufacturer. Serum globulins was calculated by
subtraction of the amount of serum albumin from the amount of total serum proteins. Concentrations of [CRP, Hp, SAA] in the serum were determined with ELISA kits according to the method described by (Sahinduran et al., 2016).

2.4. Statistical analysis: Data collected were subjected to analysis by T-independent student test to assess significant differences between groups with the aid of (SAS, 2004). All values were expressed as mean ± standard error (SE). Significance level was set at P≤0.05.

3. Results:

3.1. Clinical examination: In CPV infected dogs, very offensive bloody diarrhea, frequent vomiting, fever, depression, anorexia, weight loss with marked dehydration were the most recorded clinical signs. Confirmation of infection was done via clinic rapid CPV Ag test which gave positive results with fecal swabs (Fig. 1). Compatible thorough clinical examination reveals significant elevated body temperature, tachycardia, significant tachypnea with congested mucous membrane in CPV infected dogs compared to healthy control dogs as shown in (Table 1 & 2).

Hematological analysis: Erythrogram of CPV infected dogs, shown in (Table 3) revealed the presence of microcytic hypochromic anemia, which is marked by significant reduction in mean values of RBCs count, Hb concentration, PCV%, MCV, MCH and MCHC when compared to healthy control dogs. Where leukogram of CPV infected dogs showed significant leukopenia with marked lymphopenia and neutropenia, while total number of MID “eosinophils, basophils and monocyes” showed non-significant changes between diseased and healthy ones. Moreover, CPV infected dogs revealed significant thrombocytopenia in comparison to the mean values of healthy dogs.

3.2. Biochemical analysis: The mean values of total serum proteins, albumin, total globulins, sodium, potassium, and chloride were significantly decreased in CPV infected group than its level in healthy control dogs. On contrary the mean values of, AST, ALT, ALP, blood urea and creatinine were significantly increased in diseased dogs (Table 4).

Results of acute phase biomarkers are shown in (Table 5) Significant increase in SAA, Hp and CRP with significant reduction in mean values of serum albumin was recorded in the diseased group compared with healthy control group.

4. Discussion:

Canine Parvo viral enteritis is one of the most common destructive diseases in dogs, especially unvaccinated puppies below six months old. It is responsible for serious morbidity and mortality (Decaro et al., 2006). All examined dogs shown the characteristic clinical signs of Parvo virus infection including lethargy, anorexia, persistent vomiting, and foul-smelling diarrhea varying in color from bloody to yellow with traces of blood (Table 1, Fig. 1). This vomiting and foul-smelling bloody diarrhea is closely related to the erosive inflammatory damage of the stomach and intestinal mucosal barrier (Mccaw & Hoskins, 2006 and Streck et al., 2009).

Most of CPV infected dogs showed marked dehydration with varying degree which is marked by prolonged (CRT ≥2 seconds) values, this significant dehydration is mainly attributed to vomiting and diarrhea which is associated with large fluid and protein losses through damaged GIT (Biswas et al., 2005). Additionally, Compatible thorough clinical examination reveals significant elevated body temperature, tachycardia, significant tachypnea with congested mucous membrane in CPV infected dogs compared to healthy control dogs which comes in accordance with (AL-Hosary, 2016 and Kubesy et al., 2017). Damage to intestinal tract secondary to parvoviral infection increases markedly the risk of bacterial translocation and subsequent coliform septicemia, which may lead to development of a systemic inflammatory response syndrome (SIRS) that can progress to septic shock and ultimate death. Moreover, mortality rate was higher in puppies that met the criteria for SIRS (heart rate > 140 beats/min, respiratory rate > 30 breaths/min, temperature > 39.20 °C or < 37.80 °C) (Kalli et al., 2010).

Erythrogram of CPV infected dogs revealed the presence of microcytic hypochromic anemia; this results were compatible with that observed by (Arslan et al., 2017). This anemia might be resulted from suppression of erythropoesis through the direct inhibitory effect of CPV on bone marrow (Elayed et al., 2020) and, due to intestinal bleeding associated with loss of large volume of blood through diarrhea (Abd El-Barr et al., 2017 and Arora et al., 2018).

Where leukogram of CPV infected dogs showed significant leukopenia with marked lymphopenia and neutropenia, while total number of MID “eosinophils, basophils and monocyes” showed non-significant changes between diseased and healthy ones, as stated by (Mylonakis et al., 2016) who attributed the resultant leukocytosis changes to huge request of inflamed mucosa of intestine along with exhaustion of lymphoid tissue in addition to destruction of bone marrow precursors. However, leukocytosis and neutrophilia maybe also recorded (Kubesy et al., 2019) due to secondary bacterial infection.

In accordance with (Decaro et al., 2005) and (Shah et al., 2013) CPV infected dogs revealed significant thrombocytopenia in comparison to the mean values of healthy dogs which may attributed to loss of blood through bloody diarrhea, increased platelets utilization through infected gastrointestinal mucosa or from decreased platelets production as a direct inhibitory effect of CPV on bone marrow precursor cell.

The significant reduction in serum total protein, albumin and globulins concentration in diseased dogs was also reported by (Tefit, 2014) which resulted from anorexia with decreased food consumption and reduced protein synthesis in the liver as amino acids are shunted into synthesis of positive acute phase proteins as a body reaction to inflammation and tissue impairment which comes on the expense of albumin and other proteins synthesis (Mazzaferrro et al., 2002). Also, these results are in concurrence with those obtained by (Li and humm, 2015). This observation may be due to inadequate dietary intake, reduced absorption associated with intestinal hemorrhage and altered gastrointestinal mucosal barrier with protein losing-enteropathy. Serum values of sodium, potassium and chloride showed significant decrease in CPV infected group where these findings come in contact with (Ukwueze et al., 2020) the reduction could be attributed to poor appetite, reduced absorption from the disrupted gut with marked fluid and electrolytes loss through vomiting and diarrhea which mainly contribute to depression and general muscular weakness (Burchell et al., 2014).

The elevated ALT, AST and ALP values in diseased dogs were agreeable with those of (Kubesy et al., 2019) and (Salem, 2014). Nutritional imbalances with dehydration and hypovolemia have a strong impact on liver functions and vice versa. In this respect, increased Levels of AST, ALT and ALP activities could be attributed to hepatic hypoxia secondary to severe hypovolemia or absorption of toxic substances through disrupted gut barrier as well (Shah et al., 2013). Furthermore, highly significant increase in BUN and serum creatinine values may be due to dehydration and hypovolemia as a consequence to vomiting and diarrhea with subsequent decreased renal blood flow of affected dogs causing BUN and creatinine significantly increased (Bansanti et al., 2004). Regarding acute phase response, the obtained data showed Significant increase in positive APPs (SAA, Hp and CRP) with significant reduction in mean values of Negative APPs (serum albumin) in CPV infected dogs which is similar to those previously described by (kogika et al., 2003) and (McClure et al., 2013) who mentioned that acute phase response expression occurs at the expense of albumin synthesis in canine parvoviral enteritis as a response to severely inflamed gastrointestinal tract. In this respect these results can be explained as, during infection, hepatocytes responded by producing a large number of APPs, which are part of the innate immune system. Nowadays it is widely speculated that APPs are important components of the antimicrobial response, frequently involved directly or indirectly in the inhibition of viral replication and spread within the host body, in accordance to (Mazzaferrro, 2020).

Conclusion: This study concluded that, Canine parvoviral enteritis causing gastro-enteritis, fever and dehydration with microcytic hypochromic anemia and significant leukopenia with marked lymphopenia and neutropenia which are the main causes of death in infected animals, especially with neglected treatment and healthcare. Moreover, A typical APP response characterized by significant increase in the major (CRP and SAA) and moderate (Hp) with marked decrease in negative (albumin) APPs occurs in CPV infected dogs.
Authors contribution: IA ,MA and IE conceived and designed the study. IA performed the study. IA ,MA and IE analyzed the data. IA ,MA and IE and IA interpreted the data, IA ,MA and IE wrote the paper. IA ,MA and IE revised the final manuscript. IA ,MA and IE reviewed the manuscript.

Competing interests
There is no competing interest and we don’t have any financial support from any institutions.

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We would like from our heart to appreciate the owners of the cases.

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Fig. 1: Bloody diarrhea with positive IC rapid test kits for CPV infection.

Table (1): Clinical picture of healthy control dogs compared to CPV infected dogs:

| Parameters               | Control       | Diseased     |
|--------------------------|---------------|--------------|
| Rectal temperature °C    | 38.6±0.21     | 40.1±0.15*   |
| Respiratory rate / min.  | 21.63±1.25    | 34.22±1.12*  |
| Pulse rate / min.        | 98.2±2.29     | 129.25±2.8*  |
| Lymph nodes              | Normal        | Normal       |
| Mucous membranes         | Rosy red      | congested*   |
| CRT in seconds.          | < 2 seconds   | ≥2 seconds*  |

Table (2): Clinical manifestation scale upon presentation in CPV infected dogs:

| No.  | Clinical findings                  | No. of Dogs | Percent (%) |
|------|-----------------------------------|-------------|-------------|
| 1    | Anorexia                          | 31          | 88.57       |
| 2    | Vomiting                          | 35          | 100         |
| 3    | General Body condition:           |             |             |
|      | a. Good                           | 24          | 68.57       |
|      | b. Poor                           | 11          | 31.43       |
| 4    | Color of conjunctival mucus membrane: |          |             |
|      | a. Congested                      | 27          | 77.14       |
|      | b. Pale                           | 8           | 22.86       |
| 5    | Dehydration (%)                   |             |             |
|      | a. Mild (4-6%)                    | 8           | 22.86       |
|      | b. Moderate (6-8%)                | 22          | 62.85       |
|      | c. Severe (8-10%)                 | 5           | 14.29       |
| 6    | Body temperature:                 |             |             |
|      | a. Decreased                      | 6           | 17.14       |
|      | b. Normal                         | 11          | 31.43       |
|      | C. Increased                      | 18          | 51.43       |
Table (3): Mean values (±SE) of some hematological changes in both healthy control dogs compared to CPV infected dogs:

| Group                  | Control          | Diseased         |
|------------------------|------------------|------------------|
| RBCS (X10^6/µl)        | 6.57±0.98        | 4.48±0.34*       |
| Hb (g/dl)              | 13.69±0.86       | 10.31±0.52*      |
| PCV (%)                | 43.35±1.55       | 32.27±1.12*      |
| MCH (Pg.)              | 22.13±0.34       | 20.48±0.38*      |
| MCHC (g/dl)            | 33.80±0.53       | 27.81±0.32*      |
| MCV (fl)               | 66.76±1.96       | 60.85±0.98*      |
| WBCS (X10^3/µl)        | 12.16±1.34       | 7.16±0.91*       |
| Lymphocytes (X10^3/µl) | 3.64±0.87        | 2.01±0.66*       |
| MID(X10^3/µl)          | 1.10±0.10        | 0.98±0.09        |
| Neutrophils (X10^3/µl) | 7.42±0.63        | 4.17±0.58*       |
| Platelets (X10^3/µl)   | 427.32±6.4       | 300.61±5.15*     |

Table (4): Mean values (±SE) of some serum biochemical changes in healthy control dogs compared to CPV infected dogs:

| Group            | Control          | Diseased         |
|------------------|------------------|------------------|
| Total Proteins (g/dl) | 6.99±0.55        | 5.07±0.48*       |
| Albumin (g/dl)   | 3.98±0.16        | 2.92±0.11*       |
| Globulins (g/dl) | 3.01±0.12        | 2.15±0.14*       |
| ALT (u/l)        | 27.39±0.84       | 53.82±0.97*      |
| AST (u/l)        | 48.37±1.98       | 87.63±1.23*      |
| ALP (u/l)        | 95.72±1.6        | 176.42±5.63      |
| Na (mmol/l)      | 142.05±3.6       | 132.45±2.63*     |
| Cl (mmol/l)      | 113.43±1.52      | 102.4±1.12*      |
| K (mmol/l)       | 4.46±0.62        | 3.48±0.14*       |
| Urea (mg/dl)     | 16.39±0.74       | 39.42±0.45*      |
| Creatinine (mg/dl) | 0.87±0.26        | 3.82±0.47*       |

Table (5): Mean values (±SE) of APPs profile in both healthy Control dogs compared to CPV infected dogs:

| Group | SAA (µg/mL) | Hp (g/l) | CRP (mg/l) |
|-------|-------------|----------|------------|
| Control | 2.16±0.3 | 0.56±0.09 | 4.7±0.08 |
| CPV    | 5.91±1.16* | 2.81±0.39* | 18.45±3.5* |