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Prasanna D Hegde
Department of Veterinary Gynaecology and Obstetrics, Bengaluru, KVAFSU, Bidar, Karnataka, India

Renukaradhya GJ
Associate Professor, Department of Veterinary Gynaecology and Obstetrics, Bengaluru, KVAFSU, Bidar, Karnataka, India

Suchitra BR
Assistant Professor, Department of Veterinary Gynaecology and Obstetrics, Bengaluru, KVAFSU, Bidar, Karnataka, India-

Naveen Kumar S
Assistant Professor, Department of Animal Breeding and Genetics, Hassan, KVAFSU, Bidar, Karnataka, India

BN Nagaraj
Professor and Head, Department of Surgery and Radiology, Bengaluru, KVAFSU, Bidar, Karnataka, India

Shantha Vardhan M
Ph.D Scholar, Department of Veterinary Gynaecology and Obstetrics, Bengaluru, KVAFSU, Bidar, Karnataka, India

Corresponding Author:
Prasanna D Hegde
Department of Veterinary Gynaecology and Obstetrics, Bengaluru, KVAFSU, Bidar, Karnataka, India

Therapeutic efficacy of aglepristone and mifepristone for pyometra in dogs

Prasanna D Hegde, Renukaradhya GJ, Suchitra BR, Naveen Kumar S, BN Nagaraj and Shantha Vardhan M

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Abstract
This study evaluates the therapeutic efficacy of injectable and oral antiprogestins, alone and in combination with misoprostol, for the treatment of canine pyometra. At the Veterinary College, Hebbal, Bengaluru, from September 2023 to August 2024, 24 female dogs diagnosed with pyometra were randomly assigned to four treatment groups: Group I (aglepristone 10 mg/kg s.c. on days 0, 1, and 7), Group II (aglepristone 10 mg/kg s.c. on days 0, 1, and 7, plus misoprostol 5 µg/kg orally b.i.d. on days 2 to 6), Group III (mifepristone 5 mg/kg orally b.i.d. on days 0, 1, and 7), and Group IV (mifepristone 5 mg/kg orally b.i.d. on days 0, 1, and 7, plus misoprostol 5 µg/kg orally b.i.d. on days 2 to 6). Clinical, haematological, biochemical, and ultrasonographic parameters were assessed on days 0, 7, and 14. The incidence of pyometra was 1.40%, with higher prevalence in middle-aged (5 to 9 years, 48.57%) and nulliparous (62.38%) dogs and breeds like Labrador Retriever (14.76%), Golden Retriever (10%), and Shih Tzu (10%). Group II showed significant reductions in mean uterine lumen diameter (from 23.21±3.556 mm to 8.21±0.710 mm, $p<0.05$), globulin levels ($p<0.05$), and faster appetite recovery compared to other groups. Group IV exhibited significant reductions in neutrophil counts ($p<0.05$). No significant changes were observed in vital parameters. Injectable aglepristone with misoprostol demonstrated superior efficacy, suggesting it as an effective alternative to ovariohysterectomy for preserving fertility.

Keywords: Canine pyometra, aglepristone, mifepristone, misoprostol, antiprogestins

Introduction
Canine pyometra, a prevalent reproductive disorder in intact female dogs, occurs primarily during diestrus, characterized by pus accumulation in the uterine lumen and systemic illness (Dow, 1959; Hagman, 2022) [4, 11]. Driven by progesterone dominance and bacterial infections, predominantly *Escherichia coli*, pyometra affects approximately 20% of female dogs before age 10 years (Jitpean, 2012) [18]. Untreated, it risks severe complications like sepsis and organ failure (Hagman, 2022) [11]. Nulliparous and middle-aged dogs are particularly susceptible (Renukaradhya, 2011) [33].
Ovariohysterectomy (OHE) is the standard treatment, effectively eliminating infection but causing sterility (Fieni *et al.*, 2014) [6]. Medical alternatives, such as antiprogestins (aglepristone, mifepristone), block progesterone receptors, promote cervical relaxation, and facilitate uterine evacuation, preserving fertility (Verstegen *et al.*, 2008; Fieni, 2006) [43, 5]. This study assesses pyometra incidence and compares the efficacy of injectable aglepristone, oral mifepristone, and their combinations with misoprostol, focusing on clinical, haematological, biochemical, and ultrasonographic outcomes.

Materials and Methods
The study was conducted at the Department of Veterinary Gynecology and Obstetrics, Veterinary College, Hebbal, Bengaluru, from September 2023 to August 2024. Twenty-four female dogs diagnosed with pyometra via clinical signs (e.g., vaginal discharge, anorexia, polyuria) and ultrasonography were randomly assigned to four treatment groups (n = 6 per group): Group I: Aglepristone (10 mg/kg s.c. on days 0, 1, and 7). Group II: Aglepristone (10 mg/kg s.c. on days 0, 1, and 7) plus misoprostol (5 µg/kg orally b.i.d. on days 2 to 6). Group III: Mifepristone (5 mg/kg orally b.i.d. on days 0, 1, and 7). Group IV: Mifepristone (5 mg/kg orally b.i.d. on days 0, 1, and 7) plus misoprostol (5 µg/kg orally b.i.d. on days 2 to 6).

All groups received antibiotics and supportive therapy. Parameters assessed on days 0, 7, and 14, like Clinical: rectal temperature, heart rate, respiratory rate. Haematological: total leukocyte count (TLC), differential leukocyte count (neutrophils, lymphocytes, monocytes), total erythrocyte count (TEC), hemoglobin, and thrombocyte count. Biochemical: serum creatinine, SGPT, total protein, albumin, and globulin. Ultrasonographic: uterine lumen diameter, uterine wall thickness.

Incidence data were derived from hospital records. Statistical analysis used ANOVA for intergroup comparisons and paired t-tests for intragroup changes, with significance at $p<0.05$. Data were analysed using statistical software (SPSS).

Results

The present research was carried on to compare the therapeutic efficacy of injectable antiprogestin, oral antiprogestin alone and in combination with misoprostol for treatment of pyometra in dogs.

Mean recorded rectal temperature, Heart rate and respiratory rate of affected female dogs before and after completion of treatment were given in table 1. Given the normal physiological range of rectal temperature was 101 to 102.5 ˚F, temperature in animals of group I was 102.70±0.314 ˚F.

Pretreatment leukocytosis was observed in all groups, decreasing post-treatment, indicating reduced infection severity. Group IV showed a significant reduction in neutrophil counts (Table No. 2). No significant changes were noted in TEC, hemoglobin, or thrombocyte counts (Table 2).

Biochemical parameters (creatinine, total protein and albumin) remained within normal ranges. Group II exhibited a significant decrease in SGPT and globulin levels (from 5.050±0.1232 g/dL to 4.183±0.3208 by day 14), suggesting improved liver function and reduced inflammation (Table No. 3).

Pretreatment uterine lumen diameters were elevated (Table No. 4). Groups II and Group IV showed significant reductions post-treatment (Group II: from 23.21±3.556 mm to 8.21±0.710 mm and Group IV: from 21.52±2.167 mm to 12.08±2.054 mm, $p<0.05$). Uterine wall thickness decreased non-significantly across groups (Table No. 4, Fig. No. 1).

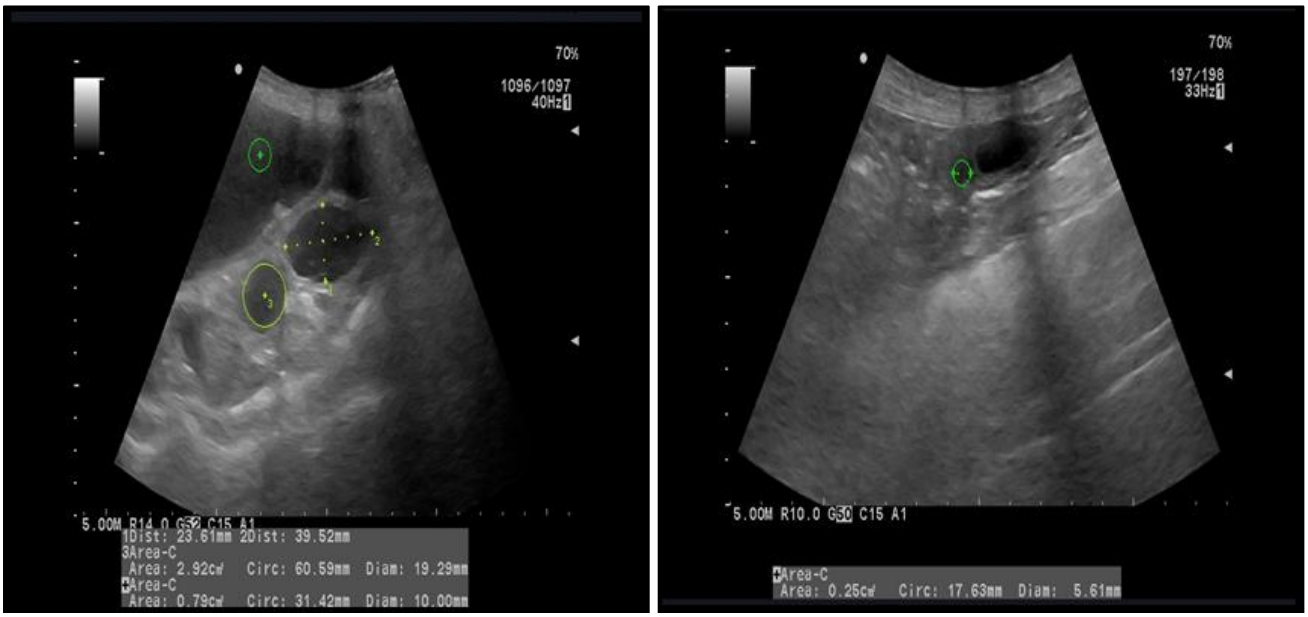

Fig 1: Mean uterine lumen diameter on Day 0and Day 14 in pyometra-treated dogs

Table 1: Changes in physiological parameters in pyometra affected dogs.

Parameter	Temperature		Heart rate (bpm)		Respiration (rate/min)	
	0th day (Pre treatment)	14th day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)
Group I	102.70±0.314	102.00±0.235	107.30±2.813	104.00±2.113	17.67±2.390^{a}	20.67±2.171
Group II	101.90±0.536	101.70±0.258	101.00±3.173	107.70±2.929	21.67±2.092^{ab}	22.67±1.764
Group III	102.10±0.321	102.00±0.280	105.20±2.833	111.00±3.286	25.67±1.202^{b}	25.50±1.668
Group IV	101.80±0.560	102.40±0.470	103.30±4.800	104.50±3.640	16.83±0.980^{Aa}	22.00±1.366^{B}

Note: Mean ± SE bearing different superscripts (lower case within column; upper case within row) are statistically different at $p<0.05$

Table 2: Haematological evaluation of pyometra affected bitches before and after Treatment

	TLC		HB		TEC		Thrombocyte count	
	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)
Group I	49.87±5.965^{a}	35.78±9.689^{a}	11.40±0.448	12.88±0.668	5.200±0.2932	6.275±0.3814^{a}	274.50±52.920	364.50±72.580
Group II	29.07±5.293^{b}	18.91±3.142^{ab}	9.83±0.650	11.55±0.889	4.533±0.3292	5.068±0.3772^{b}	198.50±81.290	342.20±92.710
Group III	36.82±7.169^{ab}	28.86±6.681^{ab}	11.22±0.714	11.50±0.651	5.162±0.2470	5.567±0.1421^{ab}	232.80±64.900	308.70±69.130
Group IV	23.52±4.833^{b}	17.43±2.478^{b}	11.15±0.961	10.95±0.804	5.007±0.3210	5.943±0.7085^{ab}	298.00±76.940	465.00±83.560

Note: Mean ± SE bearing different superscripts (lower case within column; upper case within row) are statistically different at $p<0.05$

Table 3: Serological Evaluation

	Serum creatinine		Serum SGPT		Serum total protein count		mean serum albumin count	
	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)	0 Day (Pre treatment)	14 Day (Post treatment)
Group I	1.200±0.2683	1.100±0.2129	48.28±12.060	43.94±5.615^{ab}	7.800±0.4211	7.933±0.318	2.617±0.2548	3.350±0.2592
Group II	1.063±0.1212	0.917±0.1302	27.67±0.698^{A}	50.92±6.908^{Ba}	7.750±0.4225	7.017±0.3449	2.700±0.4472	2.800±0.2805
Group III	1.183±0.1797	1.167±0.1563	46.83±8.482	52.12±7.308^{a}	7.567±0.4752	7.650±0.3128	2.717±0.3894	2.983±0.4629
Group IV	1.050±0.0619	1.000±0.0632	30.75±9.950	27.77±4.329^{b}	7.650±0.1928	7.883±0.2358	3.000±0.2608	3.600±0.4619

Note: Mean ± SE bearing different superscripts (lower case within column; upper case within row) are statistically different at $p<0.05$.

Table 4: Uterine parameters

	Mean uterine lumen diameter		Uterine wall thickness	
	0 Day (Pretreatment)	14 Day (Post treatment)	0 Day (Pretreatment)	14 Day (Post treatment)
Group I	22.54±3.013	17.08±4.760^{a}	6.265±0.4258	4.607±0.7223
Group II	23.21±3.556^{A}	8.21±0.710^{Bb}	5.243±1.4510	2.917±0.9267
Group III	18.92±2.374	14.72±2.900^{ab}	6.077±2.0870	4.623±1.7600
Group IV	21.52±2.167^{A}	12.08±2.054^{Bab}	5.468±0.2434	3.772±0.6421

Note: Mean ± SE bearing different superscripts (lower case within column; upper case within row) are statistically different at $p<0.05$

Discussion

No significant differences were observed in mean rectal temperature or heart rate across groups. This observation was same as results obtained by researchers like Unnikrishnan (2018) [41] and (Nayana 2021) [30] who reported marginal hyperthermia on the day of presentation. Sen *et al.* (2001) [35] found that the temperature was subnormal in patients having generalised toxaemia due to pyometra and normal or slightly higher in patients with open-cervix pyometra whereas, it was elevated in closed-cervix pyometra instances.

The mean respiratory rate recorded in the current investigation in different treatment protocols before, and after completion of treatment were within normal physiological range (18 to 34/min). However, statistically there was a significant difference in group IV between day 0 and day 14 Animals in three groups had a normal mean respiratory rate in the study whereas, animals in group IV had a lesser mean respiratory rate on the day of presentation which improved significantly on day 14 after the completion of treatment. Tiwari *et al.* (2004) [39] also reported shallow respiration in dogs affected with pyometra. Improvement in respiratory rate might be attributed to reduction in septicaemia and toxaemia after completion of treatment. On the contrary, Renukaradhya (2011) [33] and Unnikrishnan (2018) [41] found no difference in mean respiratory rates as in other three groups of our study.

Pretreatment leucocytosis in pyometra affected female dogs in all the four groups in our study. Canine pyometra was characterized by an inflammatory leucogram with a regenerative left shift and a marked increase in the total white blood cell count (Murugavel *et al.*, 2001; Lakshmikanth *et al.*, 2016; Hagman, 2018; Samantha *et al.*, 2018) [29, 26, 14, 34]. This could be the result of a harsh bone marrow reaction brought on by elevated immune system stress and widespread uterine suppurative inflammation in an effort to fight the infection (Sevelius *et al.*, 1990; Kustritz, 2005) [36, 20]. Similar observations of high degree of peripheral leucocytosis along with degenerative left shift with toxic neutrophils were reported (Shukla, 2012) [37].

But after the treatment protocol is initiated, there was a profound reduction in TLC among all the groups after the treatment protocol was introduced, the figures in group II and group IV nearing the normal range on day 14. These observations showed that the severity of the infection decreased as reported by Khan (2006) [23] and Prasad *et al.* (2017) [31]

The mean haemoglobin concentration in the treatment groups before the initiation of treatment were with in normal range .There was evidence of low erythrocyte count in the animals of all groups. This observation is in accordance with the observations made by Hagman *et al.* (2009) [10] and Jitpean *et al.* (2014) [19]. According to Verstegen *et al.* (2008) [43], the toxic suppression of bone marrow may be the cause of normocytic normochromic anaemia, which is characterized by a packed cell volume of 30 to 35 percent in pyometra. Canine pyometra was also associated with non-regenerative, normocytic and normochromic anaemia. This anaemia subsequently progressed to microcytic, hypochromic anaemia, the severity of which was greater in closed-cervix pyometra cases (Greene, 2006) [9].

Pyometra is a disease of chronic nature in which anaemia is caused by a variety of disorders including chronic inflammation, in which lactoferrin and other acute phase reactants mediate an iron sequestration within the myeloid cells in the bone marrow, withdrawing iron from the normal erythropoiesis.

However, it is observed that the haemoglobin and erythrocyte count returned to normal physiological range after the completion of treatment in all groups.

Thrombocytopenia occurs in pyometra cases as a result of increased consumption, decreased thrombocyte production in the bone marrow, toxic effects on the bone marrow (Fransson, 2003; Hagman, 2004) [7, 12] or increased platelet aggregating factor production mediated by endotoxin (Tsuchiya *et al.*, 1999) [40]. In current study too, initially on the day of presentation there was a lower thrombocyte concentration (within normal physiological range of 200 to 650 ($\times 10^3/mm^3$)). However, after the initiation of treatment and completion of treatment regime the mean thrombocyte concentration returned to normal range as the endotoxin production decreased.

Neutrophilia was noticed among female dogs of all the treatment groups on day 0, suggestive of inflammation. Neutrophilia in pyometra affected female dogs on the day of presentation was reported by Chinnu (2016, 82.67±1.94%) [2], Unnikrishnan (2018, 83.38±0.46%) [41] and Samantha *et al.* (2018, 84.6±5.33%) [34]. The marked neutrophilic leucocytosis with shift to left was ascribed to an aggressive bone marrow response to combat the severe bacterial

infection in pyometra (Mojzisova *et al.*, 2000) [28].

Neutrophilia reduced over the course of the treatment in the present study, reduction in neutrophil count after the initiation of treatment indicated a reduction in severity of infection, inflammation and bacterial load.

There were no significant changes in mean lymphocyte and mean monocyte count in current study as all the values within all the groups among all the days were within normal physiological range.

Many authors reported an increase in serum creatinine concentration in pyometra affected dogs (Kuplulu *et al.*, 2009; Hembram *et al.*, 2011; Jena *et al.*, 2014) [24, 15, 17], even in the present study initially there was a higher mean serum creatinine concentration. But once the treatment protocol was initiated the mean serum concentration across the groups had decreased and it was in normal physiological range.

The normal physiological range of SGPT/ ALT in healthy dogs was 12 to 118 IU/ dL. Even in the current study when the dogs were presented for examination and after the treatment protocol were completed the mean serum SGPT levels were within normal physiological range. However, there was a significant increase in SGPT level in group II from 27.67±0.698 IU/dL to 50.92±6.908 IU/dL from day 0 to day 14. This shows the effectiveness of treatment in improving the liver function as in pyometra alanine aminotransferase (ALT) levels were lowered due to hepatic membrane injury or suppression of liver enzyme synthesis, after the treatment in the study the function of liver improved due to improvement in liver enzyme production.

The mean serum total protein levels of group I, II, III and IV were found to be slightly elevated compared to normal physiological value (5.4 to 7.5g/dL). Similar elevated values were reported by Kaymaz *et al.* (1999, 7.16±0.92 g/dL) [22] and Maharathi *et al.* (2020, 8.33±0.30 g/dL) [27]. According to Singh *et al.* (2006) [38], female dogs with pyometra may have hyperproteinaemia as a result of an acute phase reaction, which is often linked to inflammation.

Mean serum albumin concentration was well within normal physiological range of 2.3 to 3.5 g/dL. All the observations in the study were under normal physiological range. However, in group IV there was a marginal increase on day 14 in mean serum albumin level. In contrary to this, hypo-albuminemia was recorded by Hagman (2012) [13] which was ascribed to albumin loss through the kidneys and increased gamma globulin synthesis (Borresen and Skrede, 1980) [1]. Reidun *et al.* (2007) [32] hypothesized that renal albumin loss was the cause of hyper-globulinemia and concurrent hypo-albuminemia.

Pre-treatment mean serum globulin (g/dL) of female dogs in group I, II, III and IV were 5.350±0.4951, 5.050±0.1232, 4.850±0.2156 and 4.650±0.3253, respectively. However, after the initiation of various treatment protocols, mean serum globulin levels decreased. As observed by Johnston *et al.* (2001) [20] dogs with pyometra were shown to have hypoalbuminemia and hyper-gammaglobulinemia. However, it is observed in the current study that after the initiation of treatment the mean globulin levels decreased. There was a significant decrease in group II from day 0 to day 14, showing the effectiveness of treatment protocol in reducing the inflammation of uterus and decreasing gamma globulin

Mean uterine lumen diameter (mm) in the present study before treatment in group I, II, III and IV were 22.54±3.013, 23.21±3.556, 18.92±2.374 and 21.52±2.167, respectively. Increased uterine diameter and wall thickness were associated with anechoic regions in the uterine lumen (Veiga *et al.*, 2017) [42]. Normal dogs had a uterine horn diameter of 6.0±0.4 mm, while dogs with pyometra had a diameter of 28.8±2.2 mm. However, there was a significant decrease in mean uterine horn diameter of animals in group II and group IV after the treatment reading 8.21±0.710 mm and 12.08±2.054 mm, respectively. This shows that inclusion of misoprostol in these two groups helped in uterine contraction and evacuation of pus from uterus, thereby decreasing the mean diameter of uterine lumen

Pre-treatment mean uterine wall thickness (mm) of animals in group I, II, III and IV were 6.265±0.4258, 5.243±1.4510, 6.077±2.0870 and 5.468±0.2434, respectively. These values indicate thickened uterine wall compared to normal healthy uterine wall thickness of 0.17±0.01 mm (Veiga *et al.*, 2017) [42]. Similar observations of thickened uterine wall in pyometra affected female dogs were observed by Vidya (2019) [44] and Unnikrishnan (2018) [41], who observed 6.0±0.44 mm and 5.79±0.15 mm, respectively.

It was noticed that there was a decrease in mean uterine wall thickness after the end of treatment on day 14 in all groups, as there was usage of antiprogestins in all groups which altered the progesterone dominance on uterine wall thereby decreasing its thickness. Even the usage of anti progestins could manage the inflammatory abnormalities of endometrium in pyometra affected female dogs (Gobello *et al.*, 2003) [8].

Group II (aglepristone plus misoprostol) showed superior efficacy, likely due to the injectable route's faster absorption and aglepristone's high progesterone receptor affinity (Hoffmann, 2000) [16]. Misoprostol's enhancement of uterine contractions and cervical relaxation facilitated pus evacuation (Danielsson, 1999) [3]. Group IV's lower efficacy may reflect mifepristone's mixed agonist/antagonist properties and oral administration challenges in vomiting dogs (Jurka, 2010) [21]. Significant reductions in globulin levels and uterine lumen diameter in Group II align with prior studies (Chinnu, 2016; Vidya, 2019) [2, 44], indicating effective inflammation reduction and uterine evacuation.

The small sample size (n = 24) limits generalizability. The lack of significant changes in some haematological parameters may reflect chronic disease adaptations. Larger, longitudinal studies are needed to optimize dosing protocols and confirm findings.

Conclusion

Injectable aglepristone combined with misoprostol offers a highly effective medical treatment for canine pyometra, significantly reducing uterine lumen diameter, globulin levels, and recovery time while preserving fertility. This approach minimizes surgical risks and economic burdens, making it a viable alternative to OHE. Further studies with larger populations are recommended.

References

1. Borresen B, Skrede S. Pyometra in the dog-a pathophysiological investigation. V. The presence of intrahepatic cholestasis and "acute phase reaction". Nord Vet Med. 1980;32:378-386.
2. Chinnu PV. Efficacy of medical management and surgical trans-cervical catheterisation for canine cystic endometrial hyperplasia. M.V.Sc thesis. Kerala

Veterinary and Animal Sciences University, Pookode, Wayanad; 2016.
3. Danielsson KG, Marions L, Rodriguez A, Spur BW, Wong PY, Bygdeman M. Comparison between oral and vaginal administration of misoprostol on uterine contractility. Obstet Gynecol. 1999;93:275-280.
4. Dow C. The cystic hyperplasia-pyometra complex in the bitch. J Comp Pathol. 1959;69:237-251.
5. Fieni F. Clinical evaluation of the use of aglepristone, with or without cloprostenol, to treat cystic endometrial hyperplasia-pyometra complex in bitches. Theriogenology. 2006;66:1550-1556.
6. Fieni F, Topie E, Gogny A. Medical treatment for pyometra in dogs. Reprod Domest Anim. 2014;49:28-32.
7. Fransson BA, Ragle CA. Canine pyometra: an update on pathogenesis and treatment. Compend Contin Educ Pract Vet. 2003;25:602-612.
8. Gobello C, Castex G, Klima L, Rodriguez R, Corrada Y. A study of two protocols combining aglepristone and cloprostenol to treat open cervix pyometra in the bitch. Theriogenology. 2003;60:901-908.
9. Greene CE. Infectious diseases of the dog and cat. 3rd ed. St. Louis: Elsevier Health Sciences; 2006. 1387 p.
10. Hagman R, Reezigt BJ, Ledin HB, Karlstam E. Blood lactate levels in 31 female dogs with pyometra. Acta Vet Scand. 2009;51:2-10.
11. Hagman R. Pyometra in small animals 2.0. Vet Clin North Am Small Anim Pract. 2022;52:631-657.
12. Hagman R. New aspects of canine pyometra: studies on epidemiology and pathogenesis. Doctoral thesis. The Swedish University of Agricultural Sciences, Uppsala, Sweden; 2004. 55 p.
13. Hagman R. Clinical and molecular characteristics of pyometra in female dogs. Reprod Domest Anim. 2012;47:323-325.
14. Hagman R. Pyometra in small animals. Vet Clin North Am Small Anim Pract. 2018;48:639-661.
15. Hembram H, Guha SK, Ghosh D. Haemato-biochemical studies in pyometra affected bitches. Indian J Anim Health. 2011;50(1):47-49.
16. Hoffmann B, Schuler G. Receptor blockers-general aspects with respect to their use in domestic animal reproduction. Anim Reprod Sci. 2000;60:295-312.
17. Jena B, Sadasivarao K, Reddy KCS. Uterine histomorphological changes in canine pyometra. J Cell Tissue Res. 2014;15(1):4747-4750.
18. Jitpean S, Hagman R, Strom Holst B. Breed variations in the incidence of pyometra and mammary tumours in Swedish dogs. Reprod Domest Anim. 2012;47(Suppl 6):347-350.
19. Jitpean S, Holst BS, Emanuelson U, Hoglund OV, Pettersson A, Alneryd Bull C, *et al.* Outcome of pyometra in female dogs and predictors of peritonitis and prolonged postoperative hospitalization in surgically treated cases. BMC Vet Res. 2014;10:6-18.
20. Johnston SD, Kustritz MVR, Olson PNS. Canine and feline theriogenology. 1st ed. Philadelphia: WB Saunders; 2001. 591 p.
21. Jurka P, Max A, Hawrynska K, Snochowski M. Age-related pregnancy results and further examination of bitches after aglepristone treatment of pyometra. Reprod Domest Anim. 2010;45:525-529.
22. Kaymaz M, Bastan A, Erunal N, Aslan S, Findik M. The use of laboratory findings in the diagnosis of CEH-Pyometra complex in the bitch. Turk J Vet Anim Sci. 1999;23:127-133.
23. Khan LAKSA. Comparative efficacy of certain therapeutic regimens in canine pyometra. M.V.Sc thesis. Maharashtra Animal and Fishery Sciences University, Nagpur; 2006. 440 p.
24. Kuplulu S, Vural MR, Demirel A, Polat M, Akcay A. The comparative evaluation of serum biochemical, haematological, bacteriological and clinical findings of dead and recovered bitches with pyometra in the postoperative process. Acta Veterinaria (Beograd). 2009;59:193-204.
25. Kustritz MVR. Cystic endometrial hyperplasia and pyometra. In: Ettinger SG, Feldman EC, editors. Textbook of Veterinary Internal Medicine. 6th ed. St. Louis: Elsevier Saunders; 2005. p. 1676-1680.
26. Lakshmikanth TR, Murthy VC, Honnappa TG, Narayanaswamy HD, Rathnamma, Kantharaj S. Physiological and hematobiochemical changes in open and closed pyometra in female dogs. Int J Appl Pure Sci Agric. 2016;2:95-97.
27. Maharathi SP, Dalai S, Mohapatra SR, Mishra APK, Mahapatra AK, Kundu IN, *et al.* Haemato-biochemical alterations in pyometra affected bitch. Int J Curr Microbiol App Sci. 2020;9:1242-1245.
28. Mojzisova J, Valocky I, Maracek I. Monitoring of selected immunological parameters in bitches with glandular cystic hyperplasia pyometra complex before and after ovariohysterectomy. Pol J Vet Sci. 2000;3:23-27.
29. Murugavel K, Senthil Kumar P, Alphonse RMD. Pyometra in Doberman bitch. Indian J Anim Reprod. 2001;22:91-93.
30. Nayana D, Becha BB, Jayakumar C, Unnikrishnan MP, Venugopal SK. Haemato-biochemical studies in medically managed open and closed-cervix pyometra in dogs. [Internet]. 2021.
31. Prasad VD, Kumar PR, Sreenu M. Pyometra in bitches: a review of literature. J Vet Sci Technol. 2017;6:12-20.
32. Reidun H, Veronica K, Jon T, Johan HJ. Renal histomorphology in dogs with pyometra and control dogs, and long-term clinical outcome with respect to signs of kidney disease. Acta Vet Scand. 2007;49:13.
33. Renukaradhya GJ. Studies on treatment of pyometra in bitches with antiprogestins. Doctoral thesis. Karnataka Veterinary, Animal and Fisheries Sciences University, Bidar; 2011.
34. Samantha G, Sarath T, Monica G, Arunmozhi N, Sridevi P, Joseph C. Ultrasonographic and haemato-biochemical evaluation of bitches affected with cystic endometrial hyperplasia-pyometra complex. Int J Curr Microbiol App Sci. 2018;7:2327-2338.
35. Sen TB, Nandi SK, Halder S. Efficacy of intamox in open cervix pyometra in canines. Intas Polivet. 2001;12:67-68.
36. Sevelius E, Tidholm A, Thoren TK. Pyometra in the dog. J Am Anim Hosp Assoc. 1990;26:33-38.
37. Shukla SP. Recent advances in canine pyometra. Indian J Canine Pract. 2012;4:25-29.
38. Singh S, Dadhich H, Sharma GD. Haemato-biochemical studies in cystic endometrial hyperplasia

pyometra complex in canine. Indian J Vet Pathol. 2006;30:46-48.
39. Tiwari SK, Roy S, Dewangan R. Pyometra with endometrial hyperplasia in two Pomeranian bitches and its surgical management. Intas Polivet. 2004;5:327-328.
40. Tsuchiya R, Kyotani K, Scott MA, Nishizono K, Ashida YT. Role of platelet activating factor in development of thrombocytopenia and neutropenia in dogs with endotoxemia. Am J Vet Res. 1999;60(2):216-221.
41. Unnikrishnan MP. Diagnosis and therapeutic management of canine pyometra for restoring breeding efficiency. Ph.D. thesis. Kerala Veterinary and Animal Sciences University, Pookode; 2018. 248 p.
42. Veiga GAL, Miziara RH, Angrimani DSR, Papa PC, Cogliati B, Vannucchi CI. Cystic endometrial hyperplasia-pyometra syndrome. [Internet]. 2017.
43. Verstegen J, Dhaliwal G, Verstegen-Onclin K. Mucometra, cystic endometrial hyperplasia, and pyometra in the bitch: advances in treatment and assessment of future reproductive success. Theriogenology. 2008;70:364-374.
44. Vidya VK. Prognostic evaluation of canine pyometra based on serum prostaglandin metabolite concentration and haematological changes. M.V.Sc thesis. Kerala Veterinary and Animal Sciences University, Pookode, Wayanad; 2019.