CLOPROSTENOL AND CABERGOLINE THERAPY IN CYSTIC ENDOMETRIAL HYPERPLASIA – PYOMETRA COMPLEX IN THE BITCHES

THESIS

Submitted

In partial fulfillment of the requirements for the Degree of

MASTER OF VETERINARY SCIENCE

IN

ANIMAL REPRODUCTION, GYNAECOLOGY & OBSTETRICS

BY

JAGYASENI MEHER

Enroll. No. V/14/294

DEPARTMENT OF ANIMAL REPRODUCTION, GYNAECOLOGY AND OBSTETRICS

NAGPUR VETERINARY COLLEGE, NAGPUR

MAHARASHTRA ANIMAL AND FISHERY SCIENCES UNIVERSITY, NAGPUR - 440006.

(INDIA)

2016
DECLARATION OF STUDENT

I hereby declare that the experimental research work and interpretation of the thesis entitled "CLOPROSTENOL AND CABERGOLINE THERAPY IN CYSTIC ENDOMETRIAL HYPERPLASIA – PYOMETRA COMPLEX IN THE BITCHES" or part thereof has not been submitted for any other degree or diploma of any University, nor the data have been derived from any thesis/publication of any University or scientific organization. The sources of materials used and all assistance received during the course of investigation have been duly acknowledged.

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This is to certify that the thesis entitled, “CLOPROSTENOL AND CABERGOLINE IN CYSTIC ENDOMETRIAL HYPERPLASIA – PYOMETRA COMPLEX IN THE BITCHES” submitted by JAGYASENI MEHER to the Maharashtra Animal and Fishery Sciences University in partial fulfillment of the requirement for the degree of MASTER OF VETERINARY SCIENCE has been approved by the Student's Advisory Committee after examination in collaboration with the External Examiner.

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First and above all, I praise God, the almighty for providing me this opportunity and granting me the capability to proceed successfully. This thesis appeared in its current form due to the assistance and guidance of several people. I would therefore like to offer my sincere thanks to all of them.

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I beg pardon to those who have helped me but their names are not appearing in this acknowledgement.

Place : Nagpur                                           (Jagyaseni Meher)

Date :
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<td>Cystic endometrial hyperplasia</td>
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<td>EDTA</td>
<td>Ethylene diamine tetra acetic acid</td>
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<td>o.i.d.</td>
<td>Once a day</td>
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<td>h</td>
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<td>ELISA</td>
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Cystic endometrial hyperplasia-pyometra complex (CEH/P) is a combination of two uterine disease conditions. One is cystic endometrial hyperplasia and the other is pyometra. Their frequent association, reflected in the naming of the condition “Cystic Endometrial Hyperplasia-Pyometra Complex”.

CEH is developed due to an exaggerated response of the uterus to chronic or repeated progestational stimulation during the luteal phase of the estrous cycle. In bitches, there is estrogen stimulation of the uterus during follicular phase of estrus cycle, followed by prolonged intervals of progesterone dominance during the luteal phase. Progesterone increases number, size and secretory activity of endometrial glands, maintains functional closure of cervix and decreases myometrial contractibility. Estrogen thought to upregulate the progesterone receptors in the endometrium thereby amplifying the progesterone effect. It’s the cyclical exposure of estrogen followed by progesterone over a number of estrus cycle, which has accumulative effect on the endometrium and the endometrium along with the cystic structures fail to regain its normal status, lead to the development of cystic endometrial hyperplasia.

In CEH, endometrial gland secretion results in an accumulation of fluid within lumen of uterus lead to hydrometra or mucometra but these conditions are sterile. However, it frequently leads to development of pyometra. Degenerative changes within the uterine tissue associated with CEH such as cystic distension of glands, fibrosis etc. along with fluid accumulation provide opportune conditions for establishment of uterine infections. Moreover, progesterone has negative effects on uterine immunity while protecting against infections. The uterus is invaded by opportunistic pathogens from the vagina into the uterus when the cervix is still open at the beginning of diestrus, which will proliferate and establish infection within the uterus and hence, development of pyometra.

The four stages of CEH-P complex are : Stage I, uncomplicated cystic endometrial hyperplasia; Stage II, cystic endometrial hyperplasia with plasma cell infiltrate (irregular cysts in endometrium); Stage III, cystic endometrial hyperplasia with acute endometritis (rougherend endometrial surface cysts and endometrial ulceration); Stage IV, cystic endometrial hyperplasia with chronic endometritis.
(Fibrotic endometrium and hypertrophic myometrium or atrophic cysts in both endometrium and myometrium) (Bigliardi et al., 2004; Smith 2006).

CEH-P complex is the most frequent and important endometrial disorder encountered in intact bitches (Bigliardi et al., 2004). It affects around one fourth of all female dogs (Verstegen et al., 2008). Of all bitches, 23.24% developed pyometra before the age of 10 years (Arnold, 2006), bitches left untreated can die and despite treatment, 4% of bitches still die (Hollinshead, 2010). Also, it predominantly affect middle-aged to older dogs (> 4 years), with mean age at presentation ranging from 6.4 to 9.5 years (Gibson et al., 2013). By that, it becomes one of the main cause of infertility, decreasing the reproductive value of important breeding bitches.

It has been well established that the most common infecting agent is *Escherichia coli*, which is isolated in 59% to 96% of pyometra cases. Occasionally, other agents (e.g., Klebsiella organisms, beta-haemolytic streptococci, coagulase-positive staphylococci, pseudomonads, Proteus, Pasteurella) are isolated from the uterus of an infected animal (Kustritz, 2005; Fransson and Ragle, 2003; Verstegen et al., 2008).

As it is a diestral disease, it is generally diagnosed from 4 weeks to 4 months after estrus. By itself, cystic endometrial hyperplasia is not associated with clinical signs. Uncomplicated CEH and mucometra may only cause the outward sign of failure to conceive due to the abnormal endometrium or sometimes causes abdominal distension. But accumulation of purulent material within the uterus i.e. the pyometra, which manifests in both local and systemic symptoms. Common clinical signs like polydipsia, polyuria, abdominal distension, vomition, anorexia, weight loss, anaemia, depression and lethargy may be observed. A purulent vaginal discharge may, however, be the only symptom in some cases of pyometra when the cervix is open. The degree of patency of the cervix dictates the severity of the clinical signs to a large extent. In closed cervix pyometra, animal becomes more seriously ill. Toxaemia or septicaemia may develop in severely affected cases.

Diagnosis of CEH-P complex cannot be done alone by clinical symptoms and history, for which ultrasonography is essential. Ultrasonographic findings
shows no or few cysts, normal endometrium and anechoic uterine content in mild cases and hypertrophic endometrium, large cysts on endometrium, irregular endometrial surface, hyperechoic uterine content in severe cases (Bigliardi et al., 2004). Diagnosis can also be supported by hemato-biochemical alterations. Haematological studies shows leucocytosis, neutrophilia with left shift, monocytosis and normocytic normochromic anaemia are common in pyometra (Verstegen et al., 2008; Shukla, 2012). Biochemical studies shows increased Alkaline phosphatase (AP), Aspartate aminotransferase (AST), globulin, total protein, BUN and creatinine levels where as decreased albumin concentration (Verstegen et al., 2008).

Ovariohysterectomy is the treatment of choice in case of CEH-P complex. The main advantage of ovariohysterectomy over medical management is that it is both curative and preventive for recurrence of pyometra. However, surgery is associated with the risk of anaesthesia. There is a risk of development of peritonitis and stump pyometra. Furthermore, medical treatment of patients presenting with pyometra prior to surgery is an option in many cases to reduce the morbidity and mortality that can be associated with immediate surgical treatment. And most importantly, as surgery is a radical form of treatment, preventing any further reproduction and renders the bitch sterile (Fieni, 2006). But there are reports which show mild type of cases can be treated successfully with medications without any surgical interventions where we can preserve the reproductive ability of valuable bitches (Gobello et al., 2003; England et al., 2007; Kempisty et al., 2013).

Natural or synthetic Prostaglandin along with antibiotic therapy are used for treatment of open cervix pyometra with appreciable results. The uterotonic action of prostaglandin, leads to a significantly faster decrease in the diameter of the uterine lumen and its luteolytic action cause a faster drop in mean plasma progesterone concentration, which prevent further endometrial thickening and degeneration. Treatment with prostaglandin, apart from its luteolytic effects, mediates functional opening of the cervix, which permits drainage of exudate, and promotes myometrial contractions, facilitating uterine drainage. Synthetic prostaglandin analogues, such as Cloprostenol, in comparison to natural Prostaglandins, are more potent in effecting luteolysis while maintaining uterotonic action (Corrada et al., 2006). Cloprostenol has a greater affinity for the
prostaglandin receptors and has a greater half-life than natural prostaglandins. The synthetic prostaglandins also cause less smooth muscle contraction, therefore resulting in fewer side effects (Eilts et al., 2002).

Cabergoline is a dopamine agonist drug which results in decreased prolactin production. Prolactin is a hormone produced by the bitch, which helps to support the corpora lutea, so that progesterone production can be maintained for an extended period of time. Repeated administration of prolactin inhibitors causes luteolysis, results in a rapid reduction of plasma progesterone concentration (Verstegen et al., 2008).

A synergistic effect on the induction of luteolysis has been suggested for the use of dopaminergic agonists and prostaglandin together. Prostaglandins have a direct action, whereas dopaminergic agonists act indirectly on the corpus luteum by withdrawing the luteotropic support provided by prolactin. The combination of these drugs would thus causes faster cervical relaxation and uterine evacuation and permits the use of lower prostaglandin doses, which is important in reducing side effects (Corrada et al., 2006).

Thus, to preserve the reproductive ability of valuable bitches, an alternative therapeutic regimen should be tested. Therefore, the present study was undertaken with the following objectives:

1. To diagnose cystic endometrial hyperplasia-pyometra complex by ultrasonography.

2. To estimate serum progesterone and haemato-biochemical parameters in cystic endometrial hyperplasia-pyometra complex bitches.

3. To study the antibiotic sensitivity of the vaginal swabs of cystic endometrial hyperplasia-pyometra complex bitches.

4. To study the efficacy of Cloprostenol and Cabergoline in cystic endometrial hyperplasia-pyometra complex bitches.
REVIEW OF LITERATURE

2.1 Diagnosis

2.1.1 Clinical signs:

Kaymaz et al. (1999) reported that clinical signs of pyometra vary with the severity and duration of the condition, occurrence of bacterial infection, the existence of endotoxemia, the patency of the cervix and the animal’s general health. The observation of symptoms such as anorexia, apathy, polyuria, polydipsia, lethargy and vomiting soon after estrous leads to suspicion of pyometra. He observed polydipsia in 85.7% and vaginal discharge in 72.2% of animal in 18 CEH-P complex bitches.

Fukuda (2001) observed clinical sign and symptoms in 25 colony raised beagle bitches with pyometra. Food intake varied among individual dogs, appetite decreased or fell off. Vomiting was not observed in any dogs. Behaviour of dogs also varied. Body temperature did not change, although some dogs showed temporarily over 39°C.

Fransson and Ragle (2003) mentioned that polyuria and polydipsia were common features of pyometra.

Roberts et al. (2003) reported that common clinical signs of CEH/pyometra included lethargy, inappetance, vomiting, diarrhoea, purulent vaginal discharge, polyuria and polydipsia. Physical examination findings commonly included dehydration, depression, body temperature change, vaginal discharge, distended and/or painful abdomen.

Zaragoza et al. (2004) reported case history and clinical findings in 15 bitches with pyometra. The clinical findings shown by proportion of animals were anorexia (86.66%), lethargy (86.66%), fever (53.33%), Dehydration (33.33%), mucous membranes (pale 20%, congested 20%), vomiting 33.33%, diarrhoea (20%), polyuria/polydipsia (86.66%) and vaginal discharge (73%).

Ravishankar et al. (2004) observed clinical signs in twenty-nine clinical cases of pyometra in bitches. Proportion of animal showing various clinical signs
and symptoms were purulent vaginal discharge (96.55%), inappetence (41.37%), vomiting (34.48%), dullness (31.03%), polydipsia (24.13%), polyuria (20.68%) and fever (10.34%).

Kustritz (2005) reported the mean prevalence of clinical signs and physical examination findings in bitches with pyometra. According to the report, the mean prevalence of clinical signs were purulent vaginal discharge 87%, lethargy 72%, anorexia 73%, polyuria/polydipsia 28%, vomiting 36% and diarrhoea 27%, respectively. Similarly, mean prevalence of physical examination findings were palpable uterine enlargement (31-40%), purulent vaginal discharge (75%), dehydration (15-28%), fever 102.5°F (41-43%) and hypothermia (3%).

Deshpande (2005) observed clinical signs and symptoms in 24 bitches with pyometra. The percentage of animal showing various signs and symptoms were vaginal discharge 100%, anorexia 94.44%, uterine distension 61.11%, vomiting 61.11%, polyuria 33.33%, polydipsia 44.44%, fever 44.44%, respiration rate (>30/min) 44.44%, lethargy 27.77%, dehydration 22.22% and diarrhoea 0%.

Khan (2006) observed clinical signs and symptoms in 24 bitches with pyometra. The percentage of animal showing various signs and symptoms were vaginal discharge 100%, anorexia 75%, uterine distension 83.33%, vomiting 33.33%, polyuria 33.33%, polydipsia 62.5%, fever 50%, lethargy 33.33%, dehydration 50% and diarrhoea 0%.

Fieni (2006) conducted a study on bitches suffering from metritis and pyometra. The general condition of bitches suffering from metritis was not altered; it remained good throughout the trial. Bitches suffering from pyometra were depressed and anorexic in (77.3%) and (64.1%) cases, respectively. On day 8, moderate lethargy and loss of appetite were observed in 17.3% and 26.9% bitches. On day 15, all bitches still receiving treatment were in good general condition, with only one showing loss of appetite.

Hagman et al. (2006a) noted clinical findings and case history in 59 bitches with pyometra and 10 bitches with CEH/mucometra. The percentage of animal showing various clinical signs in CEH/mucometra and pyometra were
polydipsia/polyuria (55% & 68%), gastrointestinal signs (11% & 70%), lethargy (11% & 64%), abdominal pain on palpation(62% & 75%), purulent-like vaginal discharge (55% & 57%), mucous membranes hyperemic or pale(0% & 23%), temperature $>39.2^\circ$C(14% & 30%), heart rate $>120$ beats/min(0% & 28%), respiratory rate $>20$ breaths/min (83% & 44%) and moderate depression (33% & 85%), respectively.

Hagman et al. (2006b) examined ten bitches suffering from pyometra. The ten pyometra patients were moderately to severely depressed, lethargic and anorectic, and had a purulent vulval discharge. Vomiting, dehydration, abnormal visible mucous membranes and polydipsia were also, but more rarely, described.

Arnold et al. (2006) reported that predominant clinical signs in bitches affected with pyometra were purulent vaginal discharge (in case of open pyometra) and polyuria / polydipsia. Bitches suffering from a closed pyometra were often presented at a later stage of the disease, when endotoxins absorbed from the uterine lumen have already resulted in a generalised illness.

Dadarwal (2007) described that in cases of cystic endometrial hyperplasia generally present with inappetance, depression, polydipsia, lethargy and abdominal distension, with (open pyometra) or vulvar discharge (closed pyometra). The vulvar discharge varied from mucoid to purulent, red- brown to yellow green and was usually foul smelling. Bitches with closed pyometra had more severe systemic signs.

Shekhar et al. (2008) performed clinical examination an eight years old German shepherd female dog with pyometra. There was a history of serosanguinus discharge with brown red pus mixed with blood, anorexia, and polydipsia. The dog was dehydrated and in shocked condition with cyanoticmucus membrane. Clinical examination revealed septicemia and elevated body temperature (103.8$^\circ$ F).

Verstegen et al. (2008) reported that the most obvious sign of canine pyometra was vaginal discharge, varied from serosanguinous to mucopurulent. Common signs include lethargy, depression and inappetance. Vomiting was
more common in the more severely affected patients. Polyuria and polydipsia were often cited as signs of pyometra and renal impairment was a feature of the disease, but these clinical signs were not consistent, being recorded in ≤50% of bitches with confirmed pyometra. Fever is not a common feature of pyometra. Dehydration was present in more advanced cases.

Singh et al. (2008) observed anorexia, dullness, depression, vomiting, polydypsia, polyuria with foul smelling pinkish vulvar discharge and abdominal pain in two German Shepherd bitches of 5 and 6 year of age with pyometra.

Pretzer (2008) discussed about clinical signs and physical exam findings in cases of cystic endometrial hyperplasia-pyometra. The most common clinical finding in bitches with open-cervix pyometra was a malodorous, sanguinous to mucopurulent vaginal discharge. Bitches with open-cervix pyometra were generally less systemically ill than bitches with closed-cervix pyometra. Additional clinical findings included lethargy, depression, inappetence/anorexia, polyuria, polydipsia, vomiting, diarrhoea. Palpable uterine enlargement was found due to fluid accumulation. Uncomplicated CEH and mucometra only caused the outward sign of failure to conceive, due to the abnormal endometrium.

Vijayanand et al. (2009) studied a 7 year old female, Spitz with cystic endometrial hyperplasia-mucometra. The bitch showed clinical signs such as inappetence, dullness, lethargy, polydipsia and weight loss since one week. Body temperature, pulse rate and heart rate were within normal range. Dehydration, abdominal distension and mucoid discharge from the external genitalia were observed. On abdominal palpation distended uterus was appreciated.

Singh et al. (2010) observed anorexia, dullness, depression, vomiting, polydipsia, polyuria and foul smelling chocolate brown to pinkish vulvar discharge in five bitches of two different breeds (3 German Shepherd and 2 Labrador) aged 5 to 8 years. Two bitches showed elevated body temperature and rest of the three bitches showed normal body temperature.

Krekeler (2010) reported that vulvar discharge varied with patency of the cervix but also presented in closed-cervix pyometra. In open-cervix pyometra,
bitches presented with more copious amounts of vulvar discharge and were less clinically ill. Vomiting and depression were often presenting complaints along with fever, polyuria/polydipsia, and abdominal distension mediated by septicaemia, bacteraemia and/or endotoxaemia.

Baithalu et al. (2010) discussed that in open cervix pyometra, bitches were less systemically ill than closed cervix pyometra. Common clinical signs included mucopurulent discharge, lethargy, depression, inappetence, polyurea, polydypsia, vomiting and diarrhoea. Fever was not present in all cases of open cervix pyometra, but in closed cervix pyometra was commonly associated with fever. Bitches with toxaemia were hypothermic. Character of vulval discharge varied in consistency and light chocolate brown in colour and malodorous. Sometimes, yellow colour and often blood tinged and watery to creamy consistency.

Lika et al. (2011) studied 15 clinical cases of canine pyometra (open type). Out of the 15 cases of open pyometra, clinical sign of vaginal discharge was shown by 15 (100%), anorexia by 11 (73.33%), polydipsia by 13 (86.66%) and vomition by 6 (40%) animals.

Gao et al. (2011) reported that dogs with CEH/pyometra exhibited symptoms such as fever, polydipsia, polyuria, abdominal distension, purulent vaginal discharge, tachycardia, tachypnea, rapid deterioration and sepsis.

Hagman et al. (2011) noted various clinical signs in 87 female dogs with pyometra. The percentage of dogs showing clinical signs were polydipsia 64%, decreased appetite 72%, moderately depressed 60%, severely depressed 26%, mild dehydration 30%, moderate dehydration 13%, severe dehydration 0%, vaginal discharge (Slight 21%, Moderate 34%, Abundant 30%).

Ucmak et al. (2012) observed clinical signs in 20 dogs with pyometra ranged in age from 3 to 16 years (mean 9.15 ± 3.65 years). The proportion of animal showing various clinical signs were vaginal discharge (75%), polyuria (90%), polydipsia (90%), vomitus (30%), dehydration (30%), abdominal extension (30%), diarrhoea (20%), and elevated body temperatures >39.2 °C (20%).
Shukla (2012) discussed that clinical signs in pyometric bitches vary with cervical patency. In cases of open cervix pyometra, the vaginal discharge was sanguineous or mucopurulent. Elevated body temperature was common feature of closed cervix pyometra while body temperature was normal or slightly elevated in open cervix pyometra. Temperature was subnormal in toxaemic cases. In advanced cases polydypsia was seen. Other symptoms included lethargy, depression, inappetence, polyuria and vomiting. Abdominal palpation in open-cervix pyometra cases revealed thickening of uterine cornua, slightly irregular and turgid structures from 1 to 3 cm in diameter.

Kumari et al. (2012) reported that three nulliparous bitches of five, six and nine years-old with pyometra were showing various sign and symptoms such as depression, passing purulent white discharge from vagina for the past 15-20 days, vomitions, polyuria, polydipsia and slight rise in body temperature.

Gupta et al. (2013a) observed clinical signs and symptoms in 9 bitches ranged from 2 to 13 years. Various clinical signs and symptoms shown by animals were vaginal discharge (66.67 %), anorexia (88.89 %), uterine distension on palpation (33.33 %), vomition (55.56 %), diarrhoea (22.22 %), polyuria (66.67 %) and polydipsia (77.78%). The colour of vaginal discharge varied from gray to chocolate with foul odour in some of the cases.

Kempisty et al. (2013) discussed that hyperplasia of the endometrium was accompanied by a light red or brownish secretion from the reproductive tract of the bitch, which was a characteristic sign of endometritis. But it depended on the extent of opening in the uterine cervix. This discharge from the reproductive tract could be observed in 80% of cases. The disease caused general signs/symptoms, such as anorexia, weakness, polydipsia/polyuria, vomiting, increased body temperature, tachycardia and tachypnoea.

Patil et al. (2013) recorded clinical signs and symptoms in 20 female dogs with pyometra. All the animals affected with pyometra had a clinical syndrome consisting of lethargy, depression, inappetence/ anorexia, polyuria, polydipsia,
vomiting and abdominal distension along with malodorous, sanguineous to muco-purulent vaginal discharge.

Jena et al. (2013b) observed elevated rectal temperature and respiration rate in 28 clinical cases of open-cervix pyometra.

Ramsingh et al. (2013) noted clinical signs in total 7 (Seven) cases of pyometra of Labrador dogs aged 6-7 years. As per the history, there were anorexia, dullness, depression, vomiting, polydysia, polyurea with slight to moderate foul smelling chocolate brown to pinkish vulvar discharge since last 3 to 5 days. The clinical examination revealed high body temperature in four and rest of the three bitches showed normal body temperature. Enlarged uterus in four bitches and uterine horn was unclear in one bitch due to tense abdomen.

Mahesh et al. (2014) noted the clinical signs in a six year old intact female German shepherd dog with closed pyometra. It had a history of inappetence, vomiting and enlarged abdomen. On clinical examination, no vaginal discharge was observed and temperature, pulse and respiratory rate were 100.2°F, 98/min and 68/min respectively.

Ros (2014a) studied clinical signs and symptoms in thirty bitches with pyometra. The percentage of animal showing various clinical signs were vaginal discharge (100%), good general condition (67%), moderately depressed (33 %), Inappetence (46%), polyuria (40%), polydipsia (30%), vomiting (25 %), diarrhoea (17%), body temperature of 39°C or above (38%), dehydration (50%), abdominal pain (52 %) and mildly hyperemic mucus membranes (7%).

Ros et al. (2014b) reported case history data and clinical examination findings of the 28 bitches with pyometra. General condition was good in 64%, moderately depressed in 36%, severely depressed in 0%. Inappetence was noted in 50%, polyuria in 39%, polydipsia in 32%, vomiting 27%, diarrhoea in 14%, body temperature >39°C in 42%, dehydration in 50%, abdominal pain in 48%, mildly hyperemic mucus membranes in 8%.

Jitpean et al. (2014) collected data on case history and clinical findings of 356 bitches of 92 different breeds diagnosed with pyometra during the years
2006–2007. Basing on the data % of animals showing various clinical signs were vaginal discharge 76.7%, anorexia 69.0%, depression 63.0%, polydipsia 61.6%, polyuria 59.4%, vomiting 21.1%, lameness 16.4%, diarrhea 15.4%, fever 31.9%, dehydration 26.4%, palpable enlarged uterus 18.8%, hyperemic mucous membranes 16.3%, pale mucous membranes 14.6% and hypothermia 4.0%.

Agrawal et al. (2015) clinically examined a five years old female German shepherd bitch with closed pyometra. It was presented with the history of vomition, polydypsia and polyuria. The clinical examination revealed that temperature, pulse and respiratory rate were 100.4°F, 97/min and 67/min respectively. The visible conjunctival mucous membrane was deeply congested indicative of toxemia and dehydration. Abdominal palpation revealed enlarged uterus and uterine horn was unclear due to tense abdomen. Vaginal examination revealed closed cervix and there was no discharge.

Schäfer-Somi (2015) reported that common uterine disorders like cystic endometrial hyperplasia (CEH), mucometra, hydrometra or pyometra were sometimes difficult to diagnose. The symptoms were often unspecific and the degree is variable. Depression of the general health status, fever, vomition, diarrhoea, polyuria / polydipsia, abdominal pain and mucopurulent, purulent or sanguinopurulent vaginal floor might be present.

Lakshmikanth et al. (2016) reported that common clinical signs of pyometra included local sign of vaginal discharge and systemic signs such as vomiting, inappetence, polyuria / polydipsia and lethargy.

Kumar et al. (2016) reported that a five year old unspayed female Labrador dog with pyometra had a history of dehydration, uterine discharge, distended abdomen, vomition, anorexia, anuria, inability to walk and pyrexia. On clinical examination, the rectal temperature was recorded as 104.9°F, with swollen vulva and pus discharge.
2.1.2 Ultrasonography:

Gabor et al. (1999) performed ultrasonography in 17 privately owned bitches of different breed with metritis or pyometra. In cases of chronic metritis & endometritis, the cross-sectional diameter of the fluid-filled uterine horns just before the cervix (measured by transabdominal ultrasonography) was less than 1.5cm (range: 0.9-1.5). In cases of open-cervix pyometra in dioestrus, the diameter of the fluid-filled uterine horns was greater than 1.5 cm (range: 1.8-2.5) as determined by ultrasonography. In cases of closed pyometra, the diameter of the fluid-filled uterine horns was greater than 1.5 cm (range 1.8-2.5). All animals were treated till their complete recovery. After recovery with medicinal treatment, the uterine diameter reduced to 0.7 (0.6-0.8) cm, 0.8 (0.7-1.0) cm and 0.8 (0.7-1.0) cm in the metritis, open and closed pyometra respectively.

Kaymaz et al. (1999) performed ultrasonography in dogs having CEH-P complex by using B–Mode Real time 3.5MHz linear transducer. In transabdominal ultrasonography, it was observed that the majority of anechogenic areas differed with the thickness of uterine wall.

Gobello et al. (2003) treated 15 bitches with the combination of Aglepristone and Cloprostenol. In the graph, it was shown that on day 1 the mean total uterine diameter laid in between 25 -30 mm. On day 3, it reduced and laid between 15-20 mm. On day 8, the mean diameters again reduced but the range remain the same as day 3. Uterine diameters diminished to normal size and the lumen was undetectable or without contents on Days 15 or 29.

Bigliardi et al. (2004) examined 45 bitches with CEH-P ultrasonography. In all cases, ultrasound examination revealed the presence of uterine exudates such as blood, mucus, pus and cystic endometrial hyperplasia. Ultrasound examination was able to clearly evaluate endometrial integrity, variation of uterine wall thickness, uterine distension and cystic endometrial glands. The glands had increased in size and number as endometrial anechoic areas (1–2 mm). In several cases, an irregular hyperplastic endometrial surface was also present. The following ultrasound classification was used: Group A: No cysts, normal endometrial surface and anechoic uterine content. Group B: Few and small cysts,
normal endometrial surface, anechoic uterine content. Group C: Many and large cysts, irregular surface and hypertrophic endometrium. Group D: Many and large cysts in all the uterus, irregular surface and hypertrophic or atrophic endometrium, hyperechoic uterine content. Mean values of uterine diameter were 2.9 cm (groups A–B), 5.5 cm (group C) and 4.7 cm (group D).

Kustritz (2005) reported that on ultrasonography CEH in bitches appeared as a fluffy, irregular, mottled thickening of the endometrium on uterine horns viewed in cross-section. CEH might not be visible in animals with distension of uterine horns caused by large volume of intrauterine fluid.

Smith et al. (2006) suggested that a fluid filled organ with variable wall thickness and proliferative changes could be visualized in canine pyometra, ultrasonographically.

Corrada et al. (2006) performed ultrasonographic examination in 29 bitches with CEH-P and measured uterine total diameter on day 1, 3, 7 and 14. The graph depicted that the mean of total uterine diameter on day 0 laid between 5-6 cm, on day 3 between 2-3 cm. The lumen became undetectable, or without abnormal contents, by Day 7 or 14.

Dadarwal (2007) discussed that ultrasonography, the preferred technique to diagnose the CEH-P complex. Uncomplicated CEH appeared as a fluffy thickening of endometrium peppered with hypoechoic areas of varying size. Extensive CEH might nearly obliterate the uterine lumen. Pyometra appeared as an enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid.

Pretzer (2008) discussed that ultrasonographic findings of canine pyometra included an enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid. The luminal contents were usually homogenous, but the contents might also be echodense with slow, swirling patterns. A thickened endometrium with cystic structures was diagnostic for CEH, with or without pyometra. Mucometra or hematometra were suspected if uterine luminal contents were echodense and hydrometra was suspected if luminal contents
were anechoic in combination with a lack of clinical signs consistent with pyometra.

Mantis (2008) reported that with pyometra, hydrometra, mucomebra or haemometra, fluid can be seen in the uterine lumen. In pyometra the fluid might be anechoic to echogenic with changes in the uterine wall and the animal may display clinical signs. In mucomebra and hydrometra the fluid was usually anechoic while in haemometra the fluid commonly was echogenic or contains echogenic foci. The appearance of the uterine fluid was not a reliable indicator for distinction of the type of fluid within the uterus. The uterine wall thickness might be increased and the wall might contain small cystic structures in cases of cystic endometrial hyperplasia that is considered a precursor to pyometra.

Davidson and Baker (2009) reported that cystic endometrial hyperplasia was characterized by endometrial thickening with focal anechoic structures noted in the uterine wall representing dilated cystic glands and tortuous glandular ducts. With advanced disease, these changes did not disappear ultrasonographically during anoestrus. Fluid accumulation in the uterine lumen might represent hydrometra, mucomebra, or developing pyometra, and can be very difficult to differentiate (echogenicity may suggest cellularity).

Domoslawska et al. (2010) estimated the uterine involution after antigestagene therapy in 12 bitches with a closed form of endometritis-pyometra complex (EPC). An average section of the uterus lumen before the treatment was 3.83 ±0.98 cm and decreased gradually until its total loss after 7-14 day. Usually, in the majority of the animals (nine bitches), the lumen loss took place up to the 7th day of the treatment. In three animals only, the end of the uterus contraction process was observed no sooner than on day 14th.

Singh et al. (2010) performed ultrasonography by B-mode, real time scanner with 7.5MHz linear array transducer in five bitches of two different breeds with pyometra. Ultrasonographic examination of these cases revealed uterine horn to be 1.5 to 3.2cm in diameter. Extensive involvement depicted round hypoechoic to anechoic area, placed side by side covering the complete abdomen while moderate involvement exhibited hypoechoic roughly round
structure ventral or ventrolateral to the anechoic urinary bladder in transverse section. Mild involvement was more readily visualized on longitudinal section as mixed anechoic to hypoechoic tubular structure.

Baithalu et al. (2010) reported that diagnosis of canine pyometra was best made with ultrasonography. Ultrasonographic findings included an enlarged uterus with convoluted, tubular horns filled with anechoic to hypoechoic fluid. The uterine wall was usually relatively hypoechoic and increase in thickness. The luminal contents were usually homogenous and filled with anechoic fluid, although small echogenic particles was identified.

Krekeler (2010) reported that in cases of canine pyometra ultrasonographic findings revealed thin-walled tubular uterus filled with hypoechoic fluid with presence or absence of flocculent material; wall could appear thick if severe CEH changes were present.

Sridevi et al. (2011) performed transabdominal ultrasonographic examinations in 31 cases of CEH in bitches where she found variable uterine wall thickness, uterine distension due to fluid accumulation and cystic dilatation of endometrial glands. In five bitches mild thickening of the endometrium with very little fluid accumulation and in six bitches the endometrium appeared thick and irregular and within the thickened endometrium were islets of anechoic foci representing dilated cystic glands. There was hypertrophy of the endometrium with irregular surface almost completely obliterating the uterine lumen and large cysts throughout the surface in 20 bitches. The anechoic/hypoechoic uterine contents were suggestive of CEH associated with pyometra.

England et al. (2007) observed fluid-filled and dilated uterus on performing ultrasound examination in 22 bitches showing clinical signs of pyometra and were treated with medication (Cloprostenol and Cabergoline). The appearance of the uterus was recorded and the internal diameter of the fluid-filled uterus was measured at the uterine body. The uterine diameter varied from slightly <2 to 6.5 cm on the day 1. There was a rapid decrease in the diameter of the uterus of all the bitches. By day 6 no fluid was detectable in the uterus of 15 of the bitches, and by day 9 no fluid was detectable in 19 of them; the other three
were treated for an extended period and by day 12, fluid was detectable only in
the bitch that did not respond. After recovery, the uterine diameters in the bitches
varied from 0 - 1 cm.

Shukla (2012) suggested that ultrasonography was a valuable aid in
diagnosis of pyometra. Uterus revealed increase in thickness (relatively
hypoechoic) and diameter and folding on itself so as many sections of each horn
may be imaged in a single plane. Uterine diameter might vary depending upon
whether the cervix was open or closed. Uterine lumen was grossly dilated with
anechoic fluid with small echogenic particles.

Kumari et al. (2012) performed ultrasonographic examination in 3
nulliparous bitches of five, six and nine years-old with open pyometra. Ultrasonographic examination revealed an anechoic area within the uterus.

Gupta et al. (2013a) performed ultrasonography in 9 bitches with
pyometra. Ultrasonographic picture revealed the echogenic fluid and hypoechoic
tubular uterus with enhancement effect due to large quantity of uterine fluid. In
some cases images showed hypoechoic enlarged uterus folded upon itself so
that the sections of both horns were visualized in a single plane, and thick
echogenic uterine wall due to increased thickness.

Ramsingh et al. (2013) performed ultrasonography of 7 labrador bitches
by B-mode, scanner with 7.5MHz linear array transducer. Ultrasonographic
examination of these cases revealed uterine horn to be 1.5 to 3.2 cm diameter.
Ultrasonographic characteristic of pyometra varied depending upon the extent of
involvement and nature of contents. Extensive involvement depicted round hypo
echoic to anechoic area, placed side by side covering the complete abdomen
while moderate involvement exhibited hypoechoic roughly round structure ventral
or ventrolateral to the anechoic urinary bladder in transverse section. Mild
involvement was more readily visualized on longitudinal section as mixed
anechoic to hypoechoic tubular structure.

Patil et al. (2013) performed ultrasonography in 20 bitches suspected for
pyometra. He found enlargement of both the uterine horns and lumen of the horn
filled with homogenous anechoic contents with the hyperechoic bands in between which gave it fluid filled like appearance.

Devi et al. (2013) performed transabdominal ultrasonographic examination of clinical cases of pyometra which revealed well defined circular or oval structure with distinct wall and a uniform hypoechoic to anechoic lumen of uterine horns. The distinct far enhancements below the anechoic loops were indicative of fluid nature of the luminal contents. The anechoic fluid inside the uterus contained homogenously distributed small hypoechoic particles. The uterine wall appeared as moderately echogenic line of varying thickness in different animals. The cross section diameter of the anechoic loops varied from 30-35.69 mm.

Younis et al. (2014) examined 12 bitches of different breeds and ages (7 months up to 13 years) by ultrasonography for CEH-P complex. Ultrasonographical examination revealed fluid filled organ with variable uterine wall thickness and proliferative changes.

Mahesh et al. (2014) performed ultrasonography in a six year old intact female German shepherd dog with pyometra, which revealed distended, anechoic to hypoechoic sacculations in both the horns.

Chandrapuria and Somil (2014) performed ultrasonography in 3 cases of pyometra (2 were Pomeranian and 1 nondescript) which revealed anechoic distended uterine horns with diameter of 2.5 to 3.5 cm.

Jena et al. (2014b) performed ultrasonographic examination in 28 bitches with pyometra. On ultrasonography, the luminal contents were usually homogenous, but in some bitches the contents were echo-dense with slow, swirling patterns. The tortuous convoluted tubules also appeared as anechoic circular structures when viewed in a transverse plane.

Batista et al. (2015) measured uterine diameter in four purebred diestrous bitches diagnosed with CEH- P complex. Uterine enlargement was confirmed by ultrasonography in all of the cases (Day 0). The Uterine Diameter in the four
bitches were Miniature Poodle (46.2mm), Shar-pei (46.3mm), Canary Dog (28mm) and Giant Schnauzer (67mm) respectively.

Agrawal et al. (2015) performed ultrasonography by B-mode, scanner with 7.5 MHZ linear array transducer in a five years old female German shepherd bitch with closed cervix pyometra. Ultrasonography depicted round hypoechoic (hypoechoic pockets depicting pus) to anechoic area.

Schäfer-Somi (2015) reported that by ultrasonography in CEH, the proliferated endometrium, multiple cysts within the uterine wall and the endometrium sometimes filling the uterine lumen as well as fluids of different amounts within the lumen could be seen. In many cases, ovarian cysts were present. In pyometra abdominal sonography will reveal an enlarged, fluid filled uterus with sometimes thickened, sometimes thinned endometrium, dependant on the degree of CEH and fluid filling.

Lakshmikanth et al. (2016) performed ultrasonography in 36 female dogs with pyometra. The ultrasound diagnosis of pyometra was arrived when there was an enlarged convoluted uterus filled with anechoic or hypo-echoic contents. The luminal contents were usually homogenous, but the contents might also be echo-dense with slow and swirling patterns.

2.1.3 Haematological values:

Kaymaz et al. (1999) studied the effects of serum biochemical profile and complete blood count in 18 bitches in the diagnosis of cystic endometrial hyperplasia (CEH)–pyometra complex. The mean of haematological parameters were RBC 5.8±1.3 (×10⁶/mm³), HCT 49±13 (%), WBC 32.05±19.5 (×10³/mm³), Hb 14.3±3.3 (g/100 ml). Blood serum biochemical results show that mean total protein (71.6±9.2 g/l) concentrations were higher than the normal levels. Mean albumin concentration (2.7±1.2 g/dl) was measured to be lower than normal values. White blood cell (WBC) levels were higher than 12x10³/mm³. The concentration of creatinine (mean: 38.7±30.4 μmol/l) and urea (mean: 40.3±26.7 mg/dl) were found to be lower than the normal levels. In 84.06% of the bitches with pyometra, serum albumin levels found to be lower than 4.1 g/dl.
Fukuda (2001) examined 25 colony-raised beagle bitches with pyometra. Blood examination showed particularly rapid elevation of leukocyte count. Simultaneously, the erythrocyte count, haemoglobin and haematocrit values decreased, while the value of plasma total protein increased. The parameters before 30 day of operation and on the day of operation were Hb [16.6±0.4 mg/dl and 12.8±0.6mg/dl], TEC [6.81±0.14 (10⁴/ml) and 5.20±0.24 (10⁴/ml)], total protein [7.5±0.2 g/dl and 8.8±0.6 g/dl] and hematocrit [47±1 % and 36±1 %], respectively. The graph depicts the TLC on 35 day before operation was < 20,000/mm³, increased to 60,000/mm³ on the day of operation and reduced to normal range after 35 days of operation.

Fransson and Ragle (2003) reported that the hematobiochemical changes in canine pyometra were leucocytosis, left shift, anemia, hypoalbuminemia, increased BUN, increased creatinine and hyperglobulinemia.

Roberts (2003) reported that complete blood count abnormalities in canine pyometra included neutrophilia with or without a left shift. Septic cases had a neutropenia, a degenerative left shift and toxic changes to the cells. Non regenerative anaemia was seen in 26% of pyometra cases. However, the CBC and differential count might be normal. Azotemia was seen in 18-26% of cases, usually from prerenal causes. Hyperproteinanaemia and hyperglobulinemia may present due to dehydration and chronic antigenic stimulation.

Bigliardi et al. (2004) studied hematobiochemical changes in CEH-P bitches. The parameters evaluated were erythrocytes (TLC), packed cell volume (HCT), leucocytes (WBC) and haemoglobin (Hb). Serum samples were analysed for urea, creatinine and total protein. The result showed neutrophilia ranging from 15 000 to 60 000/ml (means value 23 000/ml) in 75% of bitches. All other haemotological parameters were within normal range. Blood levels of creatinine were elevated while the other serum enzyme levels were normal.

Hagman (2004) studied haematobiochemical values in 20 cases of CEH in bitches. The mean of various parameters were haemoglobin (g l⁻¹) 138 ± 19.4, WBC (10⁹ l⁻¹) 10.6 ± 6.4, creatinine (μmol l⁻¹) 77 ±29, BUN(mmol l⁻¹) 4.6 ± 1.7, protein (g l⁻¹) 77 ± 6 and albumin (g l⁻¹) 31 ± 3.
Ravishankar et al. (2004) studied hematobiochemical parameters in 29 cases of CEH-P complex. Haematological studies indicated a normocytic, normochromic anaemia in 66% cases and leucocytosis with absolute neutrophilia in pyometra. Mean of haematological parameters were PCV(34.00±1.32), haemoglobin(10.91±0.42) g%, TEC (5.84±0.21) 10⁶/mm³, TLC(64.367±11.03) 10³/mm³ and differential count (neutrophil-84.65±1.9 %, lymphocyte 13.43±1.75 %, monocyte 1.26±0.61 %, eosinophil 0.65±0.23 %). Biochemical estimations revealed elevation of serum urea nitrogen, creatinine, and globulin and hypoalbuminaemia. The mean values of biochemical parameters were albumin 2.21±0.14 g/dl, globulin 5.80±0.37g/dl, creatinine 1.35±0.13 mg/dl and BUN59.98±8.19 mg/dl.

Kustritz (2005) reported that haematological changes in dogs with pyometra included changes in WBC number and anaemia. Leucocytosis, often to >30000 cells/µl, was reported to occur in 62% to 68% dogs with pyometra. A regenerative left shift and monocytosis might accompany the leucocytosis. Lymphocytopenia and anaemia of chronic infection were reported to occur in 8% to 35% and 25%of dogs with pyometra. No changes were seen in the serum chemistry profile that was pathognomonic of pyometra in dogs. Azotemia was due to dehydration and possible renal dysfunction was reported to occur in 18% to 26% of dogs with pyometra.

Deshpande (2005) performed hemato-biochemical examinations in 24 bitches with pyometra. He divided the animals into 3 equal groups. The mean of various parameters were TLC (per mm3) (34044.5±1774.16, 31005.83±2839.12 and 32538.33±3437.0), neutrophil (%) (81.06±2.13, 79.09±4.39 and 78.16±3.38), lymphocyte (%) (10.83±1.85, 11.93±3.28 and 11.76±2.42), monocyte (%) (7.12±0.88, 6.78±0.47 and 6.38±0.60), eosinophil (%) (3.89±0.16, 3.16±0.16 and 2.99±0.65), haemoglobin (gm%) (13.96±2.22, 11.73±1.09 and 14.43±1.04), BUN (mg/dl) (26.94±3.06, 19.54±1.53 and 23.03±0.96) and creatinine (mg/dl) (0.99±1.11, 1.01±0.21 and 0.61±0.14) in group I, II and III, respectively.
Khan (2006) performed hemato-biochemical examinations in 24 bitches with pyometra. He divided the animals into 4 equal groups. The mean of various parameters were TLC (381113.67±5203.54, 26908±2045.26, 31076±4350.57 and 40270.5± 7373.06) per mm3, BUN (39.93±9.51, 26.76±3.95, 30.00±3.30 and 39.95±10.06) mg/dl and creatinine (2.13±0.86, 1.30±0.24, 1.35±0.34 and 1.71±0.18)mg/dl in group I, II, III and IV, respectively.

Smith (2006) reported that elevated WBC count, prerenal azoemia, hyperproteinemia and hyperglobulinemia were the common haematobiochemical changes in canine pyometra.

Hagman et al. (2006a) studied hematobiochemical parameters in 59 bitches with pyometra and 10 bitches with CEH. The mean of haematobiochemical parameters of CEH/mucometra and pyometra patients were Hemoglobin (g l⁻¹): [137 ± 19.8 and 136 ± 24.4], WBC (10⁹ l⁻¹): [9.8 ± 2.2 and 30.2 ± 18.4], Creatinine (mmol l⁻¹): [79 ±31 and 81±42] , BUN (mmol l⁻¹):[4.6 ± 1.8 and 5.1 ± 4.0] , Protein (g l⁻¹) [76±7 and 80 ± 13] , Albumin (g l⁻¹) [30 ± 3 and 27 ± 5], respectively.

Hagman et al. (2006b) studied hematological and blood chemistry data of the 10 pyometric bitches. The mean of the parameters were: Hb (g l⁻¹) 117 ± 25, PCV (%0.34 ± 0.07, WBC (10⁹ l⁻¹) 30.2 ± 18.4, Urea (mmol l⁻¹) 3.7 ± 1.4, Creatinine (mol l⁻¹) 68 ± 14, Protein (g l⁻¹) 68 ± 7 and albumin (g l⁻¹) 19 ± 3. The results from hematological and biochemical analyses of the pyometra group were in accordance with what is considered typical in bitches with pyometra. The hyperproteinaemia in the analysed bitches with pyometra were likely to reflect an increased synthesis of acute phase proteins and antibodies in response to the bacterial infection and inflammation. There was no kidney failure judged by the normal serum urea and creatinine levels in all bitches.

Arnold et al. (2006) reported that animals affected with pyometra usually had an elevated WBC count, in many cases they also had a prerenal azotemia, hyperproteinemia and hyperglobulinemia.
England et al. (2007) estimated haematocrit, haemoglobin concentration, red blood cell count, mean corpuscular volume, mean corpuscular haemoglobin concentration, white blood cell count, and plasma progesterone, total protein and albumin concentration in 22 bitches having CEH-P complex and treated them with Cloprostenol and Cabergoline. Out of 19 open pyometric bitches, 15 had haematological abnormalities (14 had an absolute neutrophilia and one had a degenerative left shift with a mild normochromic non-regenerative anaemia), and four had biochemical abnormalities (three were hyperproteinaemic, and one was hypoproteinaemic). The three bitches with closed-cervix pyometra had haematological abnormalities (absolute neutrophilia with a mild normochromic non-regenerative anaemia) and biochemical abnormalities (one was hyperproteinaemic and two were hypoproteinaemic). When first examined, 18 of the bitches had haematological abnormalities; on day 3 only 12 had abnormalities, and by day 6 none of them had haematological abnormalities. Seven of the bitches initially had biochemical abnormalities; these had not resolved by day 3, but by day 6 only three had biochemical abnormalities, and by day 9 only the bitch that did not respond to the treatment had biochemical abnormalities.

Shekhar et al. (2008) performed hemato-biochemical examination of an eight years old German shepherd female dog. Hematological and biochemical examination revealed leucocytes (28600 /μl ), neutrophil (80 % ), lymphocyte (16 % ), eosinophil (01 % ), monocyte (03 % ), urea (41 mg/dl ) and creatinine (1.4 mg/dl ).

Verstegen et al. (2008) reported that canine pyometra cases were regarded as being accompanied by marked leukocytosis characterized by neutrophilia with a left shift and toxic degeneration of neutrophils, as well as a monocytosis. However, this was not always present, since as many as 25% of pyometra cases might have leukograms within the normal range. Many affected bitches had a mild to moderate normocytic, normochromic anemia (PCV 30–35%). Hyperproteinemia developed in response to dehydration and hyperglobulinemia reflects the chronic antigenic stimulation present with this disease. Serum blood urea nitrogen and creatinine concentrations were not
usually elevated, unless pre-renal azotemia develops as a consequence of dehydration.

Pretzer (2008) discussed that common pathologic clinical finding in bitches with pyometra was peripheral leukocytosis, which was more pronounced in closed-cervix pyometra. When a differential cell count was performed, a left shift was also a common finding. A normocytic, normochromic anemia might be seen in cases of pyometra, with packed cell volumes ranging from 21 to 48%. Abnormalities in serum chemistry include azotemia, hypergammaglobulinemia, and hypoalbuminemia.

Hagman et al. (2009) studied hemato-biochemical parameters in thirty-one privately-owned female dogs with the diagnosis of pyometra. The mean of hematobiochemical parameters were WBC \( \times 10^9 \text{l}^{-1} \) 16.8 ± 9.4, urea (mmol l\(^{-1}\)) 5.0 ± 3.2, creatinin (μmol l\(^{-1}\)) 81 ± 22, total protein (g l\(^{-1}\)) 62.4 ± 8.7, albumin (g l\(^{-1}\)) 23 ± 5, PCV (%) 37 ± 8 and haemoglobin (g/L) 124 ± 28.

Vijayanand et al. (2009) studied haematological parameters in a 7 year old female dog, with cystic endometrial hyperplasia-mucometra. Laboratory examination revealed leukocytosis characterized by neutrophilia.

Kuplulu et al. (2009) performed hematobiochemical examinations in 22 bitches with pyometra. The mean of parameters were RBC \( 10^6/μl \) 5.54±2.71, WBC \( 10^3/μl \) 35.40±5.62, HCT (%) 31.70±1.26, Band neutrophils (%) 18.54±2.56, Segment neutrophils (%) 65.77±2.65, Lymphocytes (%) 9.45±1.45, Monocytes (%) 6.40±0.88, Creatinine (mg/dl) 1.15±0.13 and BUN (mg/dl) 27.76±5.05.

Emanuelli et al. (2012) estimated hematobiochemical parameters in 12 bitches with cystic endometrial hyperplasia/pyometra and having a uterine infection caused by \( E. \text{coli} \). Hematobiochemical examination of those CEH-P animals revealed the mean of various parameters were erythrocyte: 5.02±0.92 \( (\times 10^6 \text{μL}^{-1}) \), PCV: 39.66±6.64(%), hemoglobin : 13.35±2.23(gdL\(^{-1}\)), total leukocytes : 29,441.67±15,554.04, total plasma protein: 9.34±1.08(gdL\(^{-1}\)). Erythrocyte, PCV and hemoglobin were lower, whereas total plasma protein was higher. A
leukocytosis characterized by neutrophilia with a regenerative left shift was seen. The other leukocytes had no significant alterations.

Krekeler (2010) reported that White blood cell count is most commonly > 35,000 cells/μl (neutrophilia with left shift and toxic change) finding in canine pyomera. But normoleukocytosis and leukopenia were possible and did not necessarily exclude the disease; anaemia and prerenal/ renal azotemia were common.

Baithalu et al. (2010) discussed that common clinical finding in canine pyometra was peripheral leukocytosis, often exceeding 30,000 cells/mm3, degenerative left shift with toxic neutrophils were oftenly seen. But the degree was much less marked in open cervix pyometra. A mild normocytic, normochromic non-degenerative anaemic (PCV within 30-35%) condition reflected chronic nature of disease and toxic suppression of bone marrow. The abnormal serum chemistry included hyperproteinemia and hyperglobinemia as a result of dehydration and chronic antigenic stimulation of the immune system.

Singh et al. (2010) performed haematological examination in five bitches of two different breeds with pyometra. The leucocytosis was moderate (17,000-30,000 cells / mm3) in one, marked (30,000- 50,000 cells / mm3) in two and extreme (>75,000 cells / mm3) in two bitches while neutrophil count was moderate (77- 80 %) in two, marked (> 80- 99 %) in two bitches and extreme in (>90 %) in one bitches.

Mudasir et al. (2011) investigated haematobiochemical parameters in 30 clinical cases of canine pyometra. There was significant decrease in the Hb content (10.10 ± 0.30)g% and PCV (30.42 ± 0.89) %. There was significant increase in the TLC (22.22 ± 1.13 thousand/cumm). DLC showed significant increase (P<0.05) in the number of neutrophils % (72.0 ± 0.54), significant decrease in lymphocytes % (18.09 ± 0.34) and monocytes % (2.53 ± 0.17), non-significant difference in the number of eosinophil % (5.26 ± 0.17). The mean serum creatinine (3.37 ± 0.08mg /dl) and BUN (31.04 ± 0.73mg /dl) levels were significantly higher (P<0.01) in pyometra affected bitches.
Shukla (2012) reported that leucocytosis and neutrophilia (especially in closed cervix pyometra) with regenerative shift to left and monocytes was observed in cases of closed cervix pyometra and was less marked in cases of open cervix pyometra.

Ucmak et al. (2012) investigated 20 bitches with pyometra for the effects of preoperative antibiotics and supportive therapy on hematobiochemical parameters at the 1st and 48th hour following presentation. The mean of WBC (× 10^9/μL) at the 1st and 48th hour were 38.531 ± 7.283 and 36.250 ±5.975. Similarly, means of RBC (× 10^6/μL) were 5.002 ± 0.426and 4.767 ± 0.414 ; Hb (g/dL) 10.930 ± 1.069 and 10.400± 1.052 ; HCT (%) 32.015± 2.702 and 30.060± 2.673 ; total protein (g/dL) 8.500± 0.301 and 8.500± 0.171; albumin (g/dL) 2.680 ±0.109 and 2.560 ± 0.069; urea (mg/dL) 27.600 ±6.110 and 19.770 ± 2.487 ; creatinine (mg/dL) 0.998 ±0.040 and 1.010 ± 0.038 at the 1st and 48th hour respectively. Bitches with pyometra receiving supportive therapy had no significant difference in total blood counts, or serum biochemical parameters, which were evaluated along with food intake and activity scores during the 2 day period.

Kumari et al. (2012) performed haematological examination in 3 nulliparous bitches of five, six and nine years-old with open pyometra. Hematological examination of these cases revealed considerable increase in the total white blood cell count (19,000 -50,000 cells/mm3). There was decline in hemoglobin concentration (8.95±0.37) g% along with marked neutrophilia (74.3±1.75) %.

Ramsingh et al. (2013) studied the total leucocyte count and differential leucocyte counts of total seven Labrador dogs with pyometra. The leukocytosis was moderate (16,999-29,999 cells/mm3) in one, marked (29,999-50,000 cells/mm3) in two and extreme (>75,000 cells/mm3) in two and the neutrophill % was 80% in two, marked (>80-90%) in four bitches and extreme in (>90%) in two bitches.So moderate to extreme leukocytosis and neutrophilia in these cases might help to diagnosis these cases as pyometra.

Kempisty et al. (2013) reported that in bitches with pyometra the leukocyte concentration in blood was elevated to 15 000–60 000/mm³.
Jena et al. (2013a) treated 7 clinical cases of open-cervix pyometra with a combination of Cabergoline, Cloprostenol sodium and supportive therapies. The pre-treatment (0th day) and post-treatment (8th day) mean values of haematobiochemical parameters were haemoglobin (11.10 ± 0.28 and 13.38 ± 0.33), PCV(%) (34.03 ± 0.89 and 40.83 ± 1.09), TEC(× 10⁶/μl) (5.51 ± 0.14 and 6.68 ± 0.17), TLC(× 10³/μl) (35.56 ± 8.36 and 11.46 ± 2.63), lymphocyte % (11.00 ± 1.43 and 26.14 ± 0.86), neutrophils % (78.28 ± 2.37 and 65.71 ± 0.81), monocytes %(8.43 ± 0.84 and 5.71 ± 0.28), eosinophil % (2.84 ± 0.22 and 2.43 ± 0.20), BUN (24.00 ± 0.97 and 16.43 ± 0.37)(mg/dl), creatinine (2.20 ± 0.08 and 1.60 ± 0.03)(mg/dl), total protein(8.06 ± 0.37 and 6.56 ± 0.15)(g/dl), globulin (5.21 ± 0.31 and 3.33 ± 0.16)(g/dl) and albumin (2.84 ± 0.22 and 3.23 ± 0.03)(g/dl). There was a significant increase in the levels of haemoglobin, PCV, TEC and lymphocytes. Before treatment the levels of haematological parameters like TLC, neutrophils and monocytes; biochemical parameters such as BUN, creatinine, mean total protein and globulin were higher than the normal physiological value.

Jena (2013b) studied haematological parameters in 28 bitches affected with pyometra and divided them into 4 groups. The mean of parameters were haemoglobin (g %) (11.0±0.32, 11.08±0.38, 11.08±0.42 and 11.10±0.28), PCV (%) (33.83±0.92, 34.07±1.06, 34.24±1.18 and 34.03±0.89), TEC(× 10⁶/μl) (5.48±0.17, 5.54±0.89, 5.51±0.21 and 5.51±0.14), TLC (10³/μl) (33.27±7.44, 33.44±6.89, 36.63±9.58 and 35.56±8.36), neutrophil (%) (76.86±1.06, 79.00±0.62, 79.57±1.02 and 78.28±2.37), lymphocyte (%) (11.14±0.94, 9.71±0.52, 8.86±0.74 and 11.00±1.43), monocyte (%) (9.86±0.51, 9.00±0.49, 9.00±0.31 and 8.43±0.84) and eosinophil (%) (2.14±0.40, 2.28±0.18, 2.57±0.29 and 2.28±0.28) in group I, II, III and IV, respectively. Normocytic and normochromic anaemia, leucocytosis, a predominant absolute neutrophilia, lymphopenia and monocytosis were the most common findings in all the bitches affected with pyometra.

Patil et al. (2013) performed haematological examination in 10 bitches with open pyometra and gave them medical treatment. The pre-treatment and post-treatment mean values of haematobiochemical parameters were TEC(×10⁶/μl) [4.85±1.47 and 6.31±0.94], haemoglobin (g/dl)(9.32±2.51 and 12.14±2.14), PCV (%) (29.73±8.48 and 37.46±6.14), TLC (×10³/μl)(30.45±21.72
and 15.09±8.40), neutrophil % (82.4±4.47 and 66.5±6.71), lymphocyte % (13.3±3.37% and 29.7±7.08%), monocyte % (3.5±3.23 and 2.7±2.05), total protein (g/dl) (4.78±0.89 and 7.32±1.23), albumin (g/dl) (2.57±0.57 and 3.21±0.48), creatinine (mg/dl) (2.38±1.11 and 1.64±0.52) and BUN (mg/dl) (36.45±22.86 and 23.25±7.32), respectively. There was a decrease in the total erythrocyte count (TEC), haemoglobin and packed cell volume (PCV). Leucocytosis with neutrophilia was a consistent finding. Lymphopenia, mild monocytoysis and eosinopenia was found. Biochemically, there were significant elevations of Blood urea nitrogen (BUN) and Creatinine (CRE), and decrease in protein and albumin concentration in serum.

Gupta et al. (2013b) studied the plasma biochemical profile in nine pyometric bitches. The levels of plasma urea nitrogen (60.78±10.03 mg/dl), creatinine (2.71±0.51mg/dl), plasma total protein (7.67±0.61g/dl) and globulin (5.29±0.41 g/dl) were higher, whereas albumin (2.38±0.22 g/dl) concentration was lower than normal values.

Jena et al. (2014a) were divided 14 bitches with open pyometra into two groups. Group I bitches were treated only with supportive therapies (control group). Bitches in Group II, were treated with Cloprostenol sodium with supportive therapy. The pre-treatment (0th day) and post treatment (8th day) mean values of haematobiochemical parameters of group I were haemoglobin (g%) 11.0±0.32 and 11.08±0.42, PCV (%) 33.83±0.92 and 34.24±1.18, TEC (× 10^6/μL) 5.48±0.17 and 5.51±0.21, TLC (× 10^3/μL) 33.27±7.74 and 36.63±9.58, neutrophil (%) 76.86±1.06 and 79.57±1.02, lymphocyte (%) 11.14±0.94 and 8.86±0.74, monocyte (%) 9.86±0.51 and 9.00±0.31, BUN (mg/dL) 26.28±1.47 and 24.28±1.67, creatinine (mg/dL) 2.10±0.08 and 2.06±0.09, total protein (g/dL) 7.94±0.27 and 8.10±0.39, albumin (g/dL) 2.91±0.09 and 2.93±0.13 and globulin (g/dL) 5.03±0.27 and 5.17±0.29, respectively. However, the pre-treatment (0th day) and post treatment (8th day) mean values of haematobiochemical parameters of group II were TEC (× 10^6/μL) 5.33±0.14 and 6.18±0.14, TLC (× 10^3/μL) 34.14±7.76 and 14.31±2.16, neutrophil (%) 78.00±0.97 and 69.86±0.63, lymphocyte (%) 10.00±0.92 and 20.28±0.42, monocyte (%) 10.28±0.52 and 7.43±0.20, eosinophil (%) 1.71±0.28 and 2.43±0.20, BUN (mg/dL) 29.85±1.18 and 19.28±0.36, creatinine (mg/dL) 2.18±0.06 and 1.80±0.05, total protein (g/dL)
8.13±0.24 and 7.13±0.16, albumin (g/dL) 2.93±0.11 and 3.17±0.04, globulin (g/dL) 5.20±0.27 and 3.95±0.17 respectively. The result showed return of normal blood haematological profile and serum biochemistry in all the treated bitches on 8th day of observation.

Jena et al. (2014b) estimated haematological parameters in 28 bitches with pyometra. Leucocytosis with absolute neutrophilia was the most common finding in the pyometra affected bitches. The mean Total Leukocyte Count (TLC) was found to be 34.72±7.24, (×10³/µl) and varied from 12.4 to 89.0 (×10³/µl). TLC was found to be within normal range (< 17,000 cells/mm³) in 28.57 per cent of bitches. Leucocytosis was moderate (17,000-30,000 cells/mm³) in 14.29 per cent of bitches, marked (30,000-50,000 cells/mm³) in 42.85 per cent of bitches and extreme (>50,000 cells/mm3) in 14.29 per cent of bitches. In the present study TLC was helpful in diagnosing pyometra in 71.43 per cent of the affected bitches those revealed moderate to extreme leucocytosis (>17000 cells/ mm³). The mean neutrophil count was found to be 78.68±1.32 per cent and varied from 69 to 85 percent. The neutrophil count was found to be within normal range (≤77%) in 32.14 per cent of bitches. Neutrophilia was moderate (77-79%) in 35.72 percent of bitches, marked (80-89%) in 35.72 percent of bitches, marked (80-89%) in 35.72 percent of bitches, marked (80-89%) in 35.72 percent of bitches.

Jitpean et al. (2014) collected data of 356 bitches of 92 different breeds diagnosed with pyometra during the years 2006–2007. According to that findings, percentage of animal showing various features were anemia-49.7%, neutrophilia 55.3%, leucocytosis 54.3 %, monocytes 50.7%, band neutrophils 14.9%, toxic neutrophils 9.4 %, leucopenia 3.6 %, neutropenia 3.7%, monocytopenia 3.3%, increased BUN 6.5% and increased creatinine 4.8% .

Sant’Anna et al. (2014) measured various hematobiochemical parameters in 80(group 1: 62 & group 2: 18) bitches with pyometra. The haematological and biochemical abnormalities commonly found during the course of the disease were leucocytosis with neutrophilia, hyperglobinaemia and azotemia. The mean values of haematological parameters such as erythrocyte(10⁶/mm³), PCV(%), haemoglobin (g/dl) and total leukocytes (m/mm³) were 5.58±1.44 , 36±9.52, 11.33±2.85 and 21,570 in group 1 and  6.14±1.52, 39.46±11.11 , 11.61±3.34 and 24,785 in group II, respectively. The mean values of biochemical parameters
such as albumin, total protein, BUN and creatinine were 1.9 g/dl, 9.0 g/dl, 31 mg/dl and 0.85 mg/dl in group 1 and 2.2 g/dl, 8.8 g/dl, 168 mg/dl and 2.50 mg/dl in group 2 respectively.

Mahesh et al. (2014) performed haematobiochemical examination in a six year old intact female German shepherd dog diagnosed with pyometra. Haematology revealed PCV-63%, leucocytosis with neutrophilia and predominant shift to left. Serum biochemical parameters like blood urea nitrogen (37mg/dl) and creatinine (3.6 mg/dl ) indicated renal involvement.

Ahamed et al. (2015) conducted haemato-biochemical examination of 20 bitches diagnosed positive for pyometra. The mean of various haematological and biochemical parameters were haemoglobin (Hb) 13.66 ± 0.58 gm%, Total Leucocytic Count (TLC) 15,110 ± 3026.16 (x 10^6), neutrophil (N) 66.6 ± 1.06 %, eosinophil (E) 4.7 ± 0.3 %, lymphocyte (L) 25.7 ± 1.04 %, monocyte (M) 3 ± 0.149 %, Blood Urea Nitrogen (BUN) 19.88 ± 4.91mg/dl and creatinine (CN) 2.4 ± 0.52mg/dl.

Agrawal et al. (2015) reported that haematology of a five years old female German shepherd bitch with closed pyometra revealed leucocytosis with neutrophilia and predominant shift to left.

Schäfer-Somi (2015) suggested that in cases of pyometra blood picture should be performed and in most cases would reveal leucocytosis, neutrophilia and left shift, furthermore normocytic, normochromic anemia and decreased albumin concentrations.

Mohan et al. (2015) divided a total of 36 bitches with pyometra into three groups consisting of twelve bitches in each group. The mean total erythrocyte count (million/ cmm) was (G1:4.63±0.23, G2: 4.56±0.18 and G3: 4.70± 0.20), in group I, II and III, respectively. It showed a slight increase at the end of treatment to (G1:4.75±0.25, G2:4.60±0.20 and G3: 4.85±0.26) in the respective groups. The mean of other parameters were Hb(9.20±0.50g/dl, 9.04± 0.46g/dl and 8.83±0.51g/dl),TLC (24.05±2.66, 20.45±2.59 and 20.40±2.81 per cmm), neutrophil (69.17±1.66%, 73.75±1.58% and 76.17± 3.50%)and lymphocyte
counts (9.83±0.95%, 10.08±1.13% and 12.66±0.52%) in bitches with pyometra in group I, II and III, respectively.

Kumar et al. (2016) performed hematobiochemical examinations of a five year old unspayed female Labrador dog with open cervix pyometra. Haematobiochemical profiles revealed leucocytosis with neutrophilia (78%), with slightly high serum urea nitrogen (40.90 mg/dl) and serum creatinine (2.88 mg/dl).

Lakshmikanth et al. (2016) studied the hematobiochemical changes in open pyometra in bitches. Results revealed normocytic normochromic anemia (Hb - 12.32±0.75 g% and PCV 35.95±1.99%), leucocytosis (TLC 29215.00±3466.00/cumm), neutrophilia (84.00±2.43%), lymphopenia (11.28±2.15%) and eosinopenia (1.82±0.32%). The monocyte count was (1.16±0.35%). Hyperglobulinemia (4.94±0.32 g/dl) with hypoalbuminemia (2.29±0.14 g/dl) with unaltered total protein concentration (7.22±0.22 g/dl) was consistent. The creatinine concentrations (1.40±0.23 mg/dl) were significantly higher.

2.2 Hormone estimation:

Gobello et al. (2003) treated fifteen mixed and purebred bitches with combination of aglepristine and cloprostenol & divide them basing on basal (>1.2 ng/ml) and non-basal concentration (>1.2 ng/ml). Out of 15, 6 bitches had basal concentration of progesterone and rest 9 had non-basal concentration. The bitches having non-basal concentration again divided into 2 groups and their mean were 3ng/ml and 6ng/ml. After treatment Progesterone showed a decreasing tendency in all the bitches.

Bigliardi et al. (2004) estimated serum progesterone levels in 45 bitches with CEH-P complex. Progesterone levels ranged from 2 to 25 ng/ml.

England et al. (2007) estimated plasma progesterone concentration in 22 bitches with CEH-P complex and treated with combination of Cabergoline and Cloprostenol. The plasma progesterone concentration was more than 2.0 ng/ml.
in 15 out of 19, but less than 1·0 ng/ml in rest 4 bitches having open pyometra. Out of 3 closed pyometric bitches, 1 bitch had a plasma progesterone concentration above 2·0 ng/ml, but the other two had plasma progesterone concentrations less than 1·0 ng/ml. By day 3, the plasma progesterone concentration had decreased in all 22 bitches, and it continued to decline towards basal values; by day 6, it was less than 1·0 ng/ml in all of the bitches.

Schlafer and Gifford (2008) reported that progesterone concentrations in bitches with CEH were not abnormally high.

Domoslawska et al. (2010) estimated progesterone level in 12 bitches with a closed form of endometritis-pyometra complex (EPC). The mean progesterone concentration before treatment was 34.47 ±9.54 ng/ml. It was significantly raised in all the bitches, after which it gradually decreased to low values as the after antigestagene therapy progressed. However, concentrations below 2 ng/ml were obtained no sooner than between the 7th and 14th day of the therapy.

Krekeler (2010) reported that if prostaglandins are used for treatment of canine pyometra, reduction in serum progesterone level will be within 48 hours.

Gao et al. (2011) estimated progesterone concentration in 13 endometritis, 9 pyometra bitches as well as 9 healthy bitches (5 in diestrus and 4 in estrus). The result showed the concentrations were in descending order from bitches with pyometra, bitches with endometritis, bitches in estrus and bitches in diestrus i.e. 641.00±330.00 ng/mL, 9.53±3.31ng/ml, 4.94±0.24 ng/mL and 0.52±0.29ng/ml, respectively.

Gupta et al. (2013b) studied the sex steroid profile before and after ovario-hysterectomy in nine pyometric and eight healthy bitches. Plasma progesterone profile was three times elevated vs in pyometric bitches (11.20 ± 2.88 ng/ml) than the normal ones (4.10 ± 0.91 ng/ml). It declined significantly within 8-15 days following ovario-hysterectomy.
Batista et al. (2015) estimated serum progesterone in four purebred diestrous bitches diagnosed with CEH-P. Serum Progesterone level in those four bitches were 22.1 ng/ml (Miniature Poodle), 18.5 ng/ml (Shar-pei), 25.2 ng/ml (Canary Dog), 3 ng/ml (Giant Schnauzer).

Srisuwatanasagul et al. (2006) collected blood from 6 normal bitches during dioestrus (n=6) and 6 pyometra bitches for sex steroid concentration estimation. In normal bitches the mean of progesterone concentration was 14.3 ± 10.8 ng/ml and that of the pyometric bitches was 5.8 ± 5.4 ng/ml. The results showed that the levels of steroid hormones in the normal and the pyometra group were similar.

2.3 Antibiogram:

Sahoo et al. (2005) performed bacterial isolation from 16 surgically removed uteri of pyometritis. Results showed sensitivity of Ciprofloxacin and Chloramphenicol varied in their efficacy from 63.6% to 50% and most of the isolates showed resistance to Azithromycin.

Kustritz (2005) recommended that an appropriate antibiotic choice is made based on culture and sensitivity testing of vulvar discharge. Good empiric choices for use while culture results were pending were ampicillin (22 mg/kg per os three times daily) and amoxicillin-clavulanic acid (14 mg/kg per os two times daily).

Deshpande (2005) conducted antibiotic sensitivity test of vaginal discharge from 24 pyometra cases. He found sensitivity percentage of Chloramphenicol, Neomycin and Ceftriaxone were 33.33%, 16.66% and 11.11%.

Khan (2006) conducted antibiotic sensitivity test of vaginal discharge from 24 pyometra cases. He found sensitivity percentage of Chloramphenicol and Ciprofloxacin were 50.66% and 15.55%, respectively.
Shekhar et al. (2008) collected the uterine discharge of an eight years old German shepherd female dog and subjected to antibiotic sensitivity test (ABST). ABST finding of the uterine discharge shows maximum sensitivity to Amikacin (4+).

Coggan et al. (2008) carried out microbiological isolation from the intrauterine contents of 100 dogs with pyometra. *E. coli* was the most prevalent microorganism isolated (76.6%). Considering the 151 strains of *E. coli*, 29.8% were resistant to Amicacin, 7.9% to Chloramphenicol and 6% to Neomycin. Likewise, the isolates were 75.5% sensitivite to Chloramphenicol.

Verstegen et al. (2008) suggested that identification and sensitivity should be determined from vaginal discharges as soon as possible and before initiating any antimicrobial treatment. In vitro sensitivity studies and clinical evidence suggested that Amoxicillin plus Clavulanic acid or potentiated Sulphonamides were good initial choices.

Bondade et al. (2010) conducted antibiotic sensitivity study in 12 pyometric bitches. The antibiogram of micro-organisms revealed the sensitivity of organisms for Ciprofloxacin was 55.5 %.

Krekeler (2010) reported that in cases of canine pyometra for antimicrobial therapy, culture and sensitivity should be performed but therapy had to be started at time of diagnosis. Excellent results have been achieved with Amoxicillin/Clavulanic acid, Cephalosporins and potentiated Sulfonamides

Shukla (2012) recommended to collect vulvar discharge for aerobic culture and antibiotic sensitivity test in cases of canine pyometra and to initiate treatment with antibiotic like Amoxicillin/Clavulanate and then change the antibiotic (Quinolones like Enrofloxacin or Cephalosporines) if necessary on the basis of culture sensitivity results.

Ghanbarpour and Akhtardanesh (2012) examined eighty-four *Escherichia coli* isolates from canine pyometra to detect the antibiotic resistance profiles. According to the results of antibiotic susceptibility test, the resistance rate was
11.90% and 3.57% against Streptomycin and Amoxicillin/Clavulanic acid, respectively. All of the isolates were sensitive to Ciprofloxacin.

Bassessar et al. (2013) conducted a study to determine the antibiogram of bacterial species isolated from 20 female dogs with pyometra. The antibiogram showed that sensitivity of Ciprofloxacin and Chloramphenicol were 55% and 25%, respectively.

Ros et al. (2014a) obtained cranial vaginal swab from 11 bitches and urinary samples in 2 bitches suffering from pyometra at the start of treatment for bacterial culturing. In 3 bitches the results were negative and two different bacteria were found in 2 bitches. The total resistance of cultured bacteria were Amoxicillin/Clavulanic acid 18% and Streptomycin 14%. The total sensitivity of cultured bacteria were Amoxicillin/Clavulanic acid 73% and Streptomycin 71%.

Mathew et al. (2014) conducted a study to isolate the bacteria from 17 canine pyometra samples and to find out the antibiotics which are effective against them. The overall sensitivity % of cultured bacteria were Ciprofloxacin (25%), Chloramphenicol (67%) and Ceftriaxone (17%).

Sant’Anna et al. (2014) studied the antibiotic sensitivity of uterine horn contents from 80 bitches with pyometra. Of the 80 dogs studied, 59 (73%) were positive for presence of bacteria in the uterus. The resistance and sensitivity percentages of Ciprofloxacin were 20.3% and 79.7%, respectively.

Ahamed et al. (2015) undertook microbial isolation from pus samples from 20 bitches positive for pyometra and tested the isolates for their sensitivity. Ceftriaxone + Tazobactum (71.54%), Amikacin (61.54%) were the most sensitive against E. coli isolates. In case of E. coli, resistance was observed more frequently to Amoxi-clav (53.84%) and less frequently to Ceftriaxone (15.38%) and Ciprofloxacin (30.77%). No resistance was observed in case of Amikacin. The Staphylococcus isolates were resistant to Ciprofloxacin (22.22%) and Amoxi-clav (22.22%).
Khandekar et al. (2015) isolated causative organisms from pus samples of 7 pyometra bitches. About 71.42% samples were sensitive for both Ciprofloxacin and Ceftriaxone. Streptomycin was found to have intermediate sensitivity of 57.14%.

2.4 Treatment:

2.4.1 Treatment with Cloprostenol, Cabergoline and supportive therapy:

Corrada et al. (2006) treated 29 bitches with CEH-P complex daily with Cabergoline 5 mg/kg PO and Cloprostenol 1 mg/kg SC for 7–14 days, along with supportive antibiotic and hydration therapies. Before treatment, and on Days 3, 7 and 14, all bitches were evaluated clinically and uterine horn diameter measured during trans-abdominal ultrasonography. Twenty-four of 29 bitches were cured by either Day 7 or 14. Clinical signs related to pyometra began to improve markedly as early as Day 2 of treatment. Uterine diameters decreased (P < 0.05) by Day 3 of treatment, and continued to gradually decrease, reaching normal size by Day 14. Relapses occurred in 6 of 29 cases. Pregnancy was achieved in one of the two young bitches bred after treatment. This combination of compounds was found to be an efficient and safe for treatment of CEH–P.

Gobello (2006) reported that different combinations of either natural or synthetic prostaglandins (PG) F₂α and dopamine agonists have been reported to efficiently cause luteolysis without substantial side effects. This drug combination was used for medical treatment of various stages of spontaneous pyometra, with a success rate of 82%.

England et al. (2007) treated twenty-two bitches with spontaneous pyometra with a combination of 5 μg/kg cabergoline per day and 5 μg/kg cloprostenol every third day, and potentiated sulphonamide twice a day. Bitches with either open-cervix or closed-cervix pyometra showed a rapid clinical improvement, associated with a reduction in plasma progesterone concentration, increased vulval discharge and a reduction in the diameter of the uterus. The haematological profiles of 21 of the bitches returned to normal within six days of treatment, and their biochemical profiles returned to normal within nine days; 19
of the bitches were managed successfully by a 10-day period of treatment. Eleven of the 21 successfully treated bitches were mated at the next oestrus, and seven became pregnant; their litters were smaller than the published breed averages. In four of the bitches the pyometra recurred after the next oestrus.

Mazzaferro (2010) reported that Cloprostenol could be used in cases of canine pyometra @ 1 μg/kg SC daily for 7-14 days. Cabergoline (5 μg/kg PO daily for 7 to 14 days) used with prostaglandin to increase speed of luteolysis and cervical opening.

Shukla (2012) discussed that synthetic prostaglandins (Cloprostenol; 5μg/kg every third day subcutaneously), Antiprolactin/prolactin inhibitor (Cabergoline; 5μg/kg once daily per os for 7-10 days) and antibiotics combination had been found to be successful in treating open- or closed-cervix pyometra independent of initial progesterone concentration.

Kempisty et al. (2013) recommended to treat CEH-P complex bitches with combination of Cabergoline and prostaglandin with the aim of the therapy is to decrease the concentration of serum progesterone. However, this hormonal treatment should be instituted if there was no advanced morphological lesions in the uterus and if the bitch was in a good general condition.

Jena et al. (2013a) treated 7 bitches of different breeds diagnosed as pyometra with a combination of a dopamine agonist prolactin inhibiting drug, i.e., Cabergoline @ 5μg/kg b. wt. once daily orally and lower dose of synthetic PGF2α (Cloprostenol) @ 1μg/kg b. wt. subcutaneously once daily for seven days with supportive therapies. The haematological and biochemical parameters were studied before (0th day) and after treatment (8th day). By the end of the treatment, all the hematobiochemical alterations were resolved. The recovery rate was 100%. All the treated bitches came to estrus and bred. The conception rate and recurrence rate were 71.43% and 28.57%, respectively. Combination of Cabergoline and a lower dose of Cloprostenol was found to be an effective method to treat canine pyometra.
2.4.2 Treatment with Cloprostenol and supportive therapy:

Roberts et al. (2003) reported that medical management in pyometra involved administration of prostaglandin $\text{F}_2\alpha$ either natural or synthetic (Cloprostenol). Medicinal management should be restricted to young bitches with open cervix that are not critically ill.

Fransson and Ragle (2003) recommended that a systemic bactericidal antibiotic should be administered concomitantly with PGF$_2\alpha$ to prevent bacteremia and the antibiotic treatment should be continued for 10 to 14 days. Amoxicillin (10 to 20 mg/kg PO or SC 48–12h) was a reasonable choice. The long-term outcome of medical management had been associated with recurrence in most of the dogs treated with PGF$_2\alpha$. There is a 48-hr lag before effects of treatment can be seen, and clinical deterioration can occur in the meantime.

Kustritz (2005) reported that antibiotic therapy alone was not affect a cure in dogs with pyometra. An ecbolic agent, which causes uterine contractions and promotes expulsion of the purulent fluid, must be administered concurrently. The best described ecbolic agent for use in treatment of pyometra was prostaglandin.

Smith (2006) reported that young bitches that present with an open-cervix pyometra, normal organ function, and a compliant, reasonable owner may be treated with prostaglandins in an attempt to preserve their breeding value. Many clinicians have used Cloprostenol, a prostaglandin analogue, for the treatment of open-cervix pyometra.

Arnold et al. (2006) recommended to use prostaglandins and a broad-spectrum antibiotic to treat canine pyometra.

Khan (2006) treated six pyometric bitches with Cloprostenol $\@1\mu$g/kg b. wt. IM o.i.d. upto 7 days along with antibiotics. Of the six treated bitches 5 (83.33%) were cured completely. One case did not respond; hence, it was subjected to hysterectomy.
Khan et al. (2007) treated 6 pyometric bitches with 1 μg/kg Cloprostenol im once daily for up to 7 days in combination with antimicrobials im. This group had a recovery rate of 83 % (5/6 bitches).

Mazzaferro (2010) reported that Cloprostenol can be used in cases of canine pyometra @ 1 μg/kg SC daily for 7-14 days.

Krekeler (2010) reported that Cloprostenol synthetic PGF2α analogue, slightly more expensive but less side effects; less uterine contractions than with dinoprost; reported to be 100 % effective if given at a dose of 1 μg/kg once a day for 10 days. Cloprostenol had luteolytic and ecbolic effect which facilitate evacuation of uterus.

Kumari et al. (2012) treated three nulliparous bitches having open pyometra by administering Cloprostenol @ of 5 μg/kg body weight subcutaneously every 48 hours, (Ampicillin+Cloxacillin) @ 500mg intramuscularly for seven days along with supportive therapy with Tribivet 0.5ml intramuscularly for five days and 250ml of Dextrose Normal Saline intravenously. Follow up of clinical and haematological evaluations revealed that there was a gradual improvement in hematocrit values and bitches became active and recovered well with 15 days of treatment. It was concluded that treatment with low doses of cloprostenol and the use of antibiotics was a safe and effective treatment for open pyometra.

Jena et al. (2014a) treated seven bitches with synthetic PGF2α i.e. Cloprostenol sodium at the dose rate of 1μg/kg body weight once daily for 7 days subcutaneously along with supportive therapy. The physiological parameters like rectal temperature and respiration rate, haematological parameters like total leucocyte count (TLC), neutrophil count and monocyte count and serum biochemical parameters like blood urea nitrogen (BUN), creatinine, mean total protein and globulin level which were elevated abnormally prior treatment, decreased to normal range after treatment. Other parameters such as haemoglobin, packed cell volume (PCV), total erythrocyte count (TEC), lymphocyte count and mean alanine transaminase (ALT) levels, those were at low level before treatment increased to normal range in the treatment group.
bitches in comparison with control group. There was 100 per cent recovery rate observed in the bitches treated with Cloprostenol on 8th day of therapy. The intensity of side effects was less severe. Two bitches came to estrus within 2 months of treatment and out of them one conceived on subsequent mating. In six bitches, there was recurrence of pyometra within 4 months of treatment. Recurrence rate was 85.72%. Use of cloprostenol sodium in treatment of canine pyometra in a higher dose rate for a longer duration will reduce rate of recurrence and improve the conception rate.

2.4.3 Treatment with antibiotics and supportive therapy:

Fukuda (2001) mentioned that treatments using transfusion, antibiotics, e.g. gentamicin, kanamycin, penicillin, tetracyclin, chloramphenicol, streptomycin, penicillin and prednisolone were not effective in 25 colony-raised beagle bitches with pyometra.

Singh et al. (2008) treated two German Shepherd bitches aged 5 and 6 years with pyometra Injection Intacef (Ceftriaxone X 5 days, Intramuscular- Intas) @ 20 mg/Kg body weight, Intacef (500 mg X 5 days, Intrauterine). Supportive treatment includes Injection Tribivet (Vitamin B1, B2 and B 12, 2 ml X 5 days, Intramuscular, Intas). The bitches showed complete clinical recovery after 5 days of treatment.

Singh et al. (2010) treated five plyometric bitches of two different breeds (3 German Shepherded and 2 Labrador ) aged 5 to 8 years by Injection Intacef Tazo (Ceftriaxone Sodium and Tazobactum Sodium @ 20 mg / Kg body weight for 4 - 6 days, Intramuscular), Intacef Tazo (565 mg for 4 - 6 days Intrauterine). Supportive treatment include Injection Melonex (Meloxicam, 2 ml for 3 days, Intramuscular), Injection Tribivet (Vitamin B1, B6 B12 and 2 ml for 5 days, Intramuscular). Three bitches showed complete clinical recovery after 4 days of treatment and remaining two bitches showed clinical recovery after 6 days. No reoccurrence of pyometra were reported in cured cases and 4 out of 5 cured bitches conceived when mated subsequently.
Ucmak et al. (2012) investigated the effects of preoperative supportive therapy on complete blood count, serum biochemistry parameters (total protein, albumin, urea, and creatinine) in 20 bitches with pyometra at the 12th, 24th, and 48th h following presentation. Antibiotics, multivitamin and IV fluid therapy were included in the supportive therapy. After obtaining the results, he concluded that bitches with pyometra receiving supportive therapy had no significant difference in total blood counts, or serum biochemical parameters, which were evaluated along with food intake and activity scores during the 2 day period.

Mahesh et al. (2014) treated a six year old intact female German shepherd dog with closed pyometra with antibiotics and supportive therapy. Medicinal treatment was given for one week with DNS-500ml, RL-500ml, cefotaxime sodium-500mg, dexamethasone- 4 mg, ranitidine - 1ml and metaclopramide -1ml to stabilize the patient. After one week the patient was thoroughly re-evaluated and the temperature was 102.4ºF, the blood picture revealed a leucocytic count of 8.6 millions/cmm with mild neutrophilia. PCV was found to be in the order of 42%. The visible mucous membranes became roseate but the abdominal distension remained same. Hence, radical surgery was planned instead of continuing the medicinal treatment.

Jena (2014a) treated 7 bitches with pyometra using antibiotics and supportive therapy. The author found no improvement in the values of hematobiochemical parameters on 8th day of treatment as compared to 0th day.

2.5 Side effects of Cloprostenol:

Onclin and Verstegen (1999) observed no side effects in 5 bitches treated with combination of Cloprostenol and Cabergoline.

Meter and Wright (2000) reported that administration of sodium cloprostenol in continuous low dose (1µ/kg b.wt.) produced minimal to no side effects to bitches.

Eilts (2002) reported that synthetic prostaglandin (Cloprostenol) had a greater affinity for the prostaglandin receptors and had a greater half-life than
natural prostaglandins. The synthetic prostaglandins caused less smooth muscle contraction, therefore resulting in fewer side effects. The once daily treatments of Cloprostenol provided an advantage over the every-8-hour treatments required when using the natural prostaglandin. At the low dose of 1.0 μg/kg body weight the side effects of Cloprostenol was minimum in bitches.

Roberts et al. (2003) reported that synthetic prostaglandins (Cloprostenol and Fluprostenol) were more potent than natural prostaglandins. Adverse side effects, including shock, were more likely at recommended doses in bitches.

Gobello et al. (2003) treated fifteen mixed and purebred bitches, ranging from 16 months to 15 years of age, weighing 4–50 kg, with open cervix CEH-P with Aglepristone and Cloprostenol far from feeding time was administered at the dose of 1 mg/kg S.C., None of the bitches showed either systemic or local side effects in relation to the treatment (0/15).

Fransson and Ragle (2003) reported that side effects of Cloprostenol such as anxiety, hypersalivation, panting, vomiting, abdominal pain, tachycardia, and fever were common and could be dramatic in bitches; however, they usually resolved within 1 hr after treatment. Bacteremia could occur from therapy. Two cases described in the literature of uterine rupture or peritonitis after PGF2 α treatment of bitches with closed-cervix pyometra.

Eilts (2005) discussed that side effects of Cloprostenol included vomiting, diarrhoea, but these only last about 30 minutes and was tend to wane as the treatment protocol continues. At the low dose of 1.5 μg/ kg subcutaneously, the side effects of Cloprostenol were noted to be minimal to none. In an attempt to alleviate any side effects associated with prostaglandin administration, other drugs had been added to the treatment regimen. These included atropine sulphate at the dose rate of 0.025 mg/kg, and metoclopramide at subcutaneous dose of 0.5mg/kg.

Kustritz (2005) reported side effects of prostaglandin were referable to its causing contractions of gastrointestinal tract and hypersalivation, vomition and diarrhoea.
Fieni (2006) treated 33 bitches with Cloprostenol along with Alepristine, and reported that no side effects were observed after treatment with cloprostenol in 15/33 bitches (45.5%). In the remainder, nausea was the most commonly observed side effect (12/33), and vomiting occurred in six bitches.

Corrada et al. (2006) observed side effects of Cloprostenol in 29 bitches with CEH-P. Nine of the 29 animals had mild digestive side-effects (diarrhea and vomiting not requiring treatment) after Cloprostenol administration.

Khan (2006) observed the side effects of Cloprostenol injection in 24 bitches with pyometra. Polypnoea, salivation, vomition and restlessness were observed in almost all cases with varying degree of intensity. Urination and defecation was absent in some of the cases. The side effects were observed approximately after 5 min. of Cloprostenol administration and last for near about 30 min.

England et al. (2007) reported that adverse effects of the Cloprostenol treatment in pyometrical bitches were limited to the 60 minutes immediately after the administration of prostaglandin, and included retching, vomiting, mild abdominal straining, diarrhoea and panting. The incidence of adverse effects was reduced after each successive dose of prostaglandin.

Dadarwal (2007) reported that side effects of prostaglandin therapy included panting, nausea, vomiting, diarrhoea and salivation. These side effects were seen 15-45 min after injection and decrease in severity with each subsequent dose.

Verstegen et al. (2008) reported that high doses of prostaglandins had been associated with substantial risk of uterine rupture, especially in cases of closed-cervix pyometra. Furthermore, higher doses of prostaglandins were associated with substantial adverse effects, including salivation, vomiting, straining, diarrhoea, pyrexia, some occasional respiratory distress, as well as cases of shock and death.
Mazzaferro (2010) mentioned that adverse effects of Cloprostenol in bitches were referable to contraction of smooth muscle; included hypersalivation; emesis; defecation; appeared within minutes of injection; subsided within 30 to 60 minutes; severity diminished throughout the treatment regimen; might be diminished by diluting the drug with an equal volume of sterile saline before subcutaneous injection and by walking dogs for 20 to 30 minutes after injection, antiemetics can also be utilized. Timing of feeding should avoid the hour before and the hour after PGF 2α administration to prevent vomiting of meal.

Krekeler (2010) reported that Cloprostenol synthetic PGF2α analogue, slightly more expensive but less side effects. If oral antibiotics were given care must be taken to give the drugs at a different time as the prostaglandin, which often lead to vomiting.

Jena et al. (2013a) reported percentage of animals showing various side effects after administration of Cloprostenol alone and in combination of Cabergoline in 2 different groups. There is no hypersalivation, defection and urination in any animal in either group. Percentage of animal showing side effects in Cloprostenol and in combination with Cabergoline were vomition (57.14% and 42.86%), panting (28.57% and 28.57%), restlessness (57.14% and 42.86%) and hyperpnoea (28.57% and 28.57%) respectfully.

Jena et al. (2014a) reported that after administration of Cloprostenol side effects like vomition, panting, restlessness and hyperpnoea were observed within 15 minutes and all side effects disappeared within 1 to 1.5 hours. However the intensity and severity of side effects were lower due to low dose of synthetic PGF2α analogue used for treatment. Salivation was not observed might be due to the administration of Atropine sulphate 10-15 minutes prior to administration of PGF2α. Withholding food and water supply to the bitches 4-6 hours prior to administration of PGF2α, use of Atropine sulphate and providing mild walk to bitches after PGF2α injection were practised. All these minimized the side effects by facilitating early metabolism and excretion of PGF2α end product.
MATERIALS AND METHODS

The present research work “Cloprostenol and Cabergoline Therapy in Cystic Endometrial Hyperplasia-Pyometra Complex in the Bitches “ was carried out in the Department of Animal Reproduction, Gynaecology and Obstetrics, Nagpur Veterinary College, Nagpur during the year 2015-16.

3.1 Clinical material

The bitches with complaint of pyometra presented to Teaching Veterinary Clinical Complex, Nagpur Veterinary College, Nagpur, Government Veterinary Polyclinic and Private Pet Clinics in Nagpur city were used as clinical material. The cystic endometrial hyperplasia-pyometra was diagnosed on the basis of history, symptoms, clinical examination and ultrasonographic findings. The symptoms include vaginal discharge, abdominal distension, polydipsia, polyuria, lethargy, anorexia, vomition and dehydration etc.

3.2 Ultrasonography

The diagnosis was confirmed by ultrasonography (ALOKA SSD-500). After confirmatory diagnosis 24 bitches were selected and included in the study.

A real time, B-mode portable ultrasonography with 3.5 MHz transabdominal sector transducer was used for scanning the genitalia of selected bitches. During scanning the relevant images were frozen and were captured using camera.

Preparation of Animals:

The bitches showing clinical symptoms of open cervix pyometra were prepared for ultrasonography by clipping, shaving and cleaning of ventral abdomen.

Technique of scanning:

Ultrasonography was conducted in filled urinary bladder which facilitates imaging of the uterus. All the bitches were examined in the left and right lateral as well as dorsal recumbancy. An ultrasound coupling gel was applied to abdomen and probe to increase the conductivity of ultrasound. Scanning was performed beginning from caudal end, below the urinary bladder in the prepubic region and
moving the probe cranially to scan entire abdomen. The uterus was examined to evaluate the integrity of endometrium, presence of exudates and cystic hyperplasia of endometrial glands. The widest cross-sectional diameter of uterine horns was measured by electronic calipers. The ovaries were examined to evaluate the presence of pathological changes such as cysts, neoplasia, etc.

3.3 Laboratory observations:

3.3.1 Antibiotic Sensitivity Test (AST):

Vaginal swabs were taken aseptically using sterile swabs from all selected cases. The *in vitro* antibiotic sensitivity test of the vaginal swabs was conducted as per the standard method. The swabs were inoculated in BHI broth tubes and incubated at 37°C for 12 to 24 hours. The cotton swab dipped in the broth culture tube was pressed and rotated against the inner wall of the test tube to remove excess of the bacterial suspension. The surface of pre-incubated and sterile Muller-Hinton agar (HiMedia) petri-plate was uniformly smeared with the swab, and the plate was kept at room temperature for 30 min to allow the inoculum to be adsorbed on the surface. Antibiotic sensitivity discs (Hi-Media) were placed with the help of flamed forceps on the plate at equal distance and sufficiently separated from each other. The plates were incubated at 37°C for 24hr. Antibiotics used in the present study were Amikacin, Amoxicillin/Clavulanic acid, Ampicillin / Sulbactam, Ceftriaxone, Ceftriaxone / Tazobactam, Chloramphenicol, Ciprofloxacin, Neomycin and Streptomycin. The diameter of zone of inhibition was recorded by using a Hi-media scale.

3.3.2 Hematological studies:

For haematological studies 2 ml of blood was collected from cephalic vein in EDTA (anticoagulant) containing vial. Blood samples were collected on 0\(^{th}\) day (pre-treatment), 5\(^{th}\) day (during treatment) and 10\(^{th}\) day (post treatment). The estimation of total leuakocyte count (TLC), differential leukocyte count (DLC), packed cell volume (PCV), total erythrocyte count (TEC) and haemoglobin were done by Hemo-analyser (Model ABX Micros ESV\(_{60}\), HORIBA Medical).
3.3.3 Biochemical studies:

To study the blood serum levels of BUN, creatinine, total protein, albumin and globulin, 2 ml blood was collected from cephalic vein in clot activator vial. After clotting of blood, the vial was centrifuged at 3000 rpm for 5 min. The supernatant serum was then transferred to serum collection vial and stored at -22°C till estimation of serum values of various components. For estimation semi-automated biochemical analyser (model STAR-21 Rapid Diagnostics Pvt. Ltd.) was used.

3.3.4 Hormone estimation:

To study serum progesterone level, the serum collected for biochemical studies were used. Protocols given in the product leaflet of progesterone kit (SDi Progesterone ELISA, Sigma Diagnostics) was followed. Six standards of various concentration (0, 0.5, 3, 10, 25 and 50 ng/ml), that were given in the kit were used. Absorbance of all standard and samples were obtained using ELISA reader cum spectrophotometer (Thermo Scientific) at 450nm. A standard curve was plotted using the mean absorbance of standards in excel sheet and concentration of unknown was obtained by using the standard curve.

3.4 Treatment regimens:

The confirmed 24 bitches of cystic endometrial hyperplasia-pyometra complex were divided into 3 groups, each group consisting of eight animals and were subjected to different treatment regimens as described below.

**Group I : Cloprostenol + Cabergoline + Antibiotics :**

In this group, Cloprostenol was given @ 1 µg/kg b. wt. S.C. o.i.d. for 7 days with Cabergoline @ 5 µg/kg b. wt., P.O. o.i.d. and combination of Amoxicillin and Clavulanic acid @14 mg/kg b. wt, P.O. b.i.d. till the result of AST were obtained.

**Group II : Cloprostenol + Antibiotics :**

In this group, Cloprostenol was given @ 1 µg/kg b.wt. S.C. o.i.d. for 7 days and combination of Amoxicillin and Clavulanic acid @14mg /kg b. wt., P.O. b.i.d. till the result of AST were obtained.
Group III : Antibiotics :

In this group, combination of Amoxicillin and Clavulanic acid @ 14 mg/kg b. wt. P.O. b.i.d. till the result of AST were obtained.

Depending upon AST results different antibiotics used for treatment were considered to be single entity as broad spectrum antibiotics for the sake of interpretation of the results. Supportive therapy was given as per the merit of individual case.

3.5 Drug used:

Inj. Cloprostenol

Trade name: Repregna (Vet Mankind, New Delhi)

Content: Cloprostenol sodium

Each ml of Repregna contains cloprostenol sodium 263 mcg equivalent to cloprostenol 250mcg.

Tab. Cabergoline

Trade name: Cabgolin (Sun Pharmaceutical Idustries Ltd., Mumbai)

Content: Cabergoline

Each tablet of Cabgolin contains cabergoline 0.5 mg of cabergoline.

Inj. Atropine Sulphate

Trade name: AT-VET (M/s DOTCOM PHARMA, Mumbai)

Content: Atropine Sulphate

Each ml of AT-VET contains Atropine Sulphate 1 mg.

Inj. Metoclopramide

Trade name: Perinorm (IPCA Laboratories Ltd., Mumbai)

Content: Metoclopramide

Each ml of Metoclopramide contains Metoclopramide 5mg/ml.
Tab. Amoxycillin + Clavulanic Acid

Trade name: Clavet (Cipla Ltd, Mumbai)

Content: Amoxycillin and Clavulanic acid

Each tablet contains Amoxycillin 400mg and Clavulanic acid 100mg.

3.6 Mechanism of action of drugs used:

**Cloprostenol**: It is a synthetic prostaglandin, a luteolytic agent cause regression of corpus luteum and arrests its secretory activity, thereby decreasing serum progesterone level. It has a direct stimulating effect on uterine smooth muscle causing contraction and a relaxant effect on the cervix, thereby evacuation of pus content takes place.

**Cabergoline**: It is a long acting Dopamine D2 agonist which selectively inhibits prolactin by hypothalamic inhibitory control exerted through dopamine release. By withdrawing the luteotropic support provided by prolactin, it indirectly helps in luteolysis.

**Atropine sulphate**: it is an anticolinergic (parasympatholytic) agent that completely blocks the muscarinic receptors in peripheral tissues of smooth muscles, bronchial muscles, heart, iris and secretory glands. Bronchial smooth muscles are relaxed producing bronchodilation. It relaxes smooth muscles of gut and reduces the glandular secretions. Thereby, it reduces the side effects such as defecation, vomition and hyperpnoea due to bronchoconstriction.

**Metoclopramide**: It has specific Dopamine antagonistic action blocking the Dopamine receptors which induce emesis. It also increases gastric motility and emptying the gastric contents to posterior segment.

**Amoxicillin + Clavulanic Acid**: Potassium clavulanate is a beta-lactamase resistant beta-lactam. It inhibits betalactamases produced by some microorganisms and makes them susceptible to Amoxicillin which itself is hydrolysed by betalactamases.
3.7 Post Treatment Observations (Side effects of drug used):

Bitches treated with Cloprostenol were kept under observations for about 1 hour for its side effects. The side effects were recorded in the treated bitches such as salivation, vomition, defecation, urination, depression, hyperpnoea and restlessness.

3.8 Statistical analysis:

Data collected in the present study were analysed by Completely Randomized Block Design.
RESULTS AND DISCUSSION

The present research work “Cloprostenol and Cabergoline in cystic endometrial hyperplasia -pyometra complex in the bitches” was carried out in the Department of Animal Reproduction, Gynaecology and Obstetrics, Nagpur Veterinary College, Nagpur during the year 2015-16. Female dogs presented to Teaching Veterinary Clinical Complex, Government Veterinary Polyclinic and Private Pet Clinics in Nagpur city were included in the present study. A total of twenty four bitches were selected on the basis of history, symptoms, clinical examination and ultrasonographic findings, and were divided into 3 equal groups. Group I treated with Cloprostenol, Cabergoline, antibiotics and supportive therapy. Group II treated with Cloprostenol, antibiotics and supportive therapy. Group III treated with antibiotics and supportive therapy only. The antibiotics were given as per the antibiotics sensitivity results. Hematobiochemical examinations, ultrasonographic examination and progesterone estimation were undertaken on 0th, 5th and 10th day to support the diagnosis and assess the efficacy of treatment regimens chosen for present study.

4.1 Clinical Signs:

Clinical signs and symptoms observed during the present study are presented in Table 1.

Table 1. Number and Percentage of different clinical symptoms in cystic endometrial hyperplasia- pyometra complex

<table>
<thead>
<tr>
<th>Particulars</th>
<th>Number of affected bitches showing symptoms</th>
<th>Percentages (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal discharge</td>
<td>24</td>
<td>100</td>
</tr>
<tr>
<td>Anorexia</td>
<td>18</td>
<td>75</td>
</tr>
<tr>
<td>Hyperpnoea (RR&gt;30/min)</td>
<td>16</td>
<td>66.66</td>
</tr>
<tr>
<td>Dehydration</td>
<td>11</td>
<td>45.83</td>
</tr>
<tr>
<td>Hyperemic mucous membrane</td>
<td>10</td>
<td>41.66</td>
</tr>
<tr>
<td>Fever (temp.&gt; 102.5°C)</td>
<td>8</td>
<td>33.33</td>
</tr>
</tbody>
</table>
Table 1 shows that in the present study, the percentage of clinical signs of vaginal discharge was 100%, anorexia 75%, hyperpnoea (RR>30/min) 66.66%, dehydration 45.83%, hyperemic mucous membrane 41.66%. Fever (temp.>102.5°C), polydipsia and depression were shown by 33.33% bitches, polyuria by 29.16%, palpable enlarged uterus 20.83%, pale mucous membrane 16.66%, vomiting by 16.66%, lameness 8.33%, diarrhoea & hypothermia 4.16% and tachycardia (HR>120/min) 0%.

The clinical signs of the present investigation are in close agreement with Krustritz (2005) and Jitpean et al. (2014). Krustritz (2005) reported the mean prevalence of purulent vaginal discharge to be 87%, lethargy 72%, anorexia 73%, polyuria/polydipsia 28%, vomiting 36% and diarrhoea 27%. Jitpean et al. (2014) reported vaginal discharge to be 76.7%, anorexia 69.0%, depression 63.0%, polydipsia 61.6%, polyuria 59.4%, vomiting 21.1%, lameness 16.4%, diarrhea 15.4%, fever 31.9%, dehydration 26.4%, palpable enlarged uterus 18.8%, hyperemic mucous membranes 16.3%, pale mucous membranes 14.6% and hypothermia 4.0%.

Lika et al. (2009) and Ravishankar et al. (2004) reported clinical symptom of vaginal discharge to be 100% and 96.55% respectively. These values are in close agreement with the present finding. Finding of anorexia is in agreement with Zaragoza et al. (2004), Lika et al. (2009), Hagman et al. (2011) who reported it to be 86.66%, 73.33% and 72%, respectively. Findings of polyuria and
Plate 1. Uterine discharge before treatment

Plate 2. Cessation of uterine discharge after treatment
polydipsia are in close agreement with Ravishankar et al. (2004), Krustritz (2005) and Ros et al. (2014a). Ravishankar et al. (2004) and Hagman et al. (2006a) reported 31.03% and 33% clinical symptoms of depression which are in close agreement with the present finding. Hagman et al. (2011) reported dehydration in 43% animals which is similar to the present finding. Jitpean et al. (2014) noted fever in 31.9% and hypothermia in 4.0% of animals which supports the findings of the present study.

The nature of vaginal discharge varied (mucopurulent or sero-sanguineous) from case to case. In group I and II vaginal discharge increase after 24-48 hours after 1st dose of Cloprostenol, continue for 1-2 days and then regressed. It might be due to smooth muscle contraction and cervical relaxation facilitated by Cloprostenol, both of which promote uterine evacuation. Polyuria, polydipsia, fever, dehydration, hyperpnoea and depression were of mild to moderate degree.

4.2 Ultrasonographic findings:

Among the available diagnostic imaging tools, real time ultrasound provides a valuable, non-invasive and economically feasible method of examining the status of reproductive organs of bitches. It can potentially distinguish between normal and abnormal uterine status. It is an efficient procedure for the qualitative and quantitative examination and diagnosis of CEH-P in bitches. It provides important information concerning uterine wall thickness and composition (presence of cystic structures), lumen size and content (fluid accumulation), and overall organ symmetry and position. Therefore, in the present study ultrasonography was used for diagnosis of CEH-P and confirmation of post-treatment recovery.

Ultrasonographic examinations of bitches were conducted on 0th day (Pre-treatment), 5th day (during treatment) and 10th day (post-treatment). During which the observations and uterine diameter were noted.

Ultrasonographic examination prior to treatment in bitches revealed anechoic areas in the uterine lumen indicating fluid filled uterus and hypoechoic uterine wall with varying degree of thickness i.e. the cystic endometrial hyperplasia. In 16 cases, mild thickening of the endometrium, normal endometrial
surface and homogenous anechoic uterine content was found. In 6 cases, uterine contents were hypoechoic and small echogenic particles were identified within the content with (4/6) or without (2/6) swirling pattern movement of uterine content. In 2 cases, relatively more endometrial thickening with few small cysts, normal endometrial surface with hypoechoic fluid accumulation in uterine lumen. In most of the cases, uterine horn enlargement was symmetrical. In 4 cases, segmental distension (compartmentalization) of uterine horns was observed. Uterine diameters were noted ≥1.4 cm and ≤ 3.1 cm in all cases. Cervix was identified as hyperechoic with os open in all cases. Ovaries were identified in four cases, out of which in three cases it was found to be normal and in one case, both ovaries showed anechoic areas indicating ovarian cysts. In other cases, ovaries could not be visualised probably due to smaller size and gas filled intestinal loops causing obstruction to the ultrasound path.

The present findings are in agreement with those of Baithalu et al. (2010) who reported that the hypoechoic and increase in thickness of uterine wall, whereas the luminal contents were usually homogenous and filled with anechoic fluid, although small echogenic particles may be identified. The sonographic findings of present study is similar to findings of group A (No cysts, normal endometrial surface and anechoic uterine content) and group B (Few and small cysts, normal endometrial surface, anechoic uterine content) of CEH-P reported by Bigliardi et al. (2004). Krekeler (2010) reported that CEH-P appeared as hypoechoic fluid with presence or absence of flocculent material and thick uterine wall. Jena et al. (2014b) reported that in pyometra the luminal contents were usually homogenous, but in some bitches the contents were echo-dense with slow, swirling patterns.

The ultrasound findings after completion of treatment schedule revealed reduction in diameter of uterine lumen and thickness of uterine wall which indicated positive response to the treatment.

The 0th, 5th and 10th day uterine diameters were presented in Table 2 and Fig 1.
Table 2. Uterine diameter (cm) in different groups of bitches (Mean±S.E.)

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>2.35±0.2a</td>
<td>1.01±0.08bd</td>
<td>0.68±0.05bb</td>
<td>0.381</td>
<td>0.518</td>
</tr>
<tr>
<td>Group II</td>
<td>2.17±0.17ab</td>
<td>1.23±0.07bc</td>
<td>0.92±0.03bc</td>
<td>0.326</td>
<td>0.444</td>
</tr>
<tr>
<td>Group III</td>
<td>2.27±0.16a</td>
<td>2.12±0.15A</td>
<td>2.08±0.15A</td>
<td>0.324</td>
<td>0.285</td>
</tr>
<tr>
<td>CD 5%</td>
<td>0.441</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td>0.387</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly.

In group I, the mean uterine diameter on 0th day was 2.35±0.2 cm. Significant reduction was seen to 1.01±0.08 cm and 0.68±0.05 cm on 5th and 10th day, respectively. However, the reduction was not significant from 5th day to 10th day.

In group II, the mean uterine diameter on 0th day was 2.17±0.17 cm. The values significantly reduced to 1.23±0.07 cm and 0.92±0.03 cm on 5th and 10th day, respectively. However, significant difference was not found between 5th and 10th day.

In group III, the mean uterine diameter on 0th, 5th and 10th day were 2.27±0.16 cm, 2.12±0.15 cm and 2.08±0.15 cm. No significant difference was seen between the days.

There was no significant difference noticed on 0th day between the groups. As there was improvement in group I and II, the difference became significant on 5th and 10th day from group III. However, there was no significant difference between group I and II on the same day.

The 0th day values are in tune with Gabor et al. (1999), Gobello et al. (2003) and Ramsingh et al. (2013) who reported the range of uterine diameter to be 1.8-2.5 cm, 2.5-3.0 cm and 1.5-3.2 cm on day 1, respectively. Other researchers including Bigliardi et al. (2004) and England et al. (2011) found the upper range up to 7 cm which is higher than present findings.
Plate 3. Anechoic luminal content, endometrial hyperplasia with uterine diameter (3.1cm) on 0\textsuperscript{th} day in Group-I

Plate 4. Reduced endometrial hyperplasia with uterine diameter (1.17cm) on 5\textsuperscript{th} day in Group-I

Plate 5. Normal endometrium with uterine diameter (0.57cm) on 10\textsuperscript{th} day in Group-I
The 10th day findings are in tune with Gabor et al. (1999) who found the range of uterine diameter to be 0.6 to 1.0 cm after recovery and England et al. (2007) 0-1 cm after recovery on day 6, 9 and 12 in different animals. However, Fieni (2006) reported that the uterine lumen became non-detectable ultrasonographically after complete recovery.

The significant reduction in diameter in group I and II was may be due to faster evacuation of uterine content after Cloprostenol administration. Moreover, in group I Cabergoline supports Cloprostenol in luteolysis and uterine evacuation which rendered faster reduction in uterine diameter than group II.

4.3 Laboratory findings :

4.3.1 Antimicrobial sensitivity of Uterine discharge in CEH-P complex :

On 0th day, vaginal swabs were collected from all the selected bitches aseptically before giving any treatment and subjected to Antibiotic Sensitivity Test immediately. Results of AST were represented in Table 3 and Fig 2.

Table 3. Antimicrobial sensitivity and Degree of sensitivity of uterine discharge to different antibiotics

<table>
<thead>
<tr>
<th>Name of antimicrobial drug</th>
<th>Number of uterine sample subjected to test</th>
<th>Degree of sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitive (%)</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanic acid</td>
<td>24</td>
<td>75</td>
</tr>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>24</td>
<td>64.28</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>24</td>
<td>64.28</td>
</tr>
<tr>
<td>Ceftriaxone/Tazobactam</td>
<td>24</td>
<td>62.5</td>
</tr>
<tr>
<td>Amikacin</td>
<td>24</td>
<td>41.66</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>24</td>
<td>37.5</td>
</tr>
<tr>
<td>Neomycin</td>
<td>24</td>
<td>20.84</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>
Fig 1. Mean Uterine Diameter (cm) in different groups of bitches on different days

Fig 2. Sensitivity (%) of uterine discharge to different Antibiotics
In the present study, Amoxicillin/Clavulanic acid was found to be the most effective antibiotic to which 75% samples were sensitive. Ampicillin/Sulbactam, Chloramphenicol and Ceftriaxone/Tazobactam showed sensitivity against 64.28%, 64.28% and 62.5% of samples respectively. Sensitivity to a lesser fraction of samples i.e. 41.66%, 37.5% and 20.84% were shown by Amikacin, Ciprofloxacin and Neomycin respectively. Ceftriaxone and Streptomycin showed resistance against all the samples.

The present findings are in close agreement with Ros et al. (2014a) who reported that 73% of the cultured bacteria were sensitive to Amoxicillin/Clavulanic acid whereas Ghanbarpour and Akhtardanesh (2012) were found Amoxicillin/Clavulanic acid to have a resistance of 3.57%. Mathew et al. (2014) reported that sensitivity of Chloramphenicol was 67% which supports the present findings. Shekhar et al. (2008) reported that Amikacin had maximum sensitivity and Ahamed et al. (2015) reported that Amikacin had a sensitivity of 61.54%. These findings differ from the present findings. Sahoo et al. (2005), Bassessar et al. (2013) and Bondade et al. (2010) reported sensitivity of Ciprofloxacin in between 65% to 50%. Mathew et al. (2014) found Ciprofloxacin had a sensitivity of 25%. In the present finding, Ciprofloxacin showed 37.5% sensitivity which lie in between the above findings. The Neomycin sensitivity of present finding is in accordance with Deshpande (2005) who reported it to be 16.66%. Coggan et al. (2008) reported 6% resistance in case of neomycin whereas finding of this study showed it to be 79.16% which is much higher than Coggan’s finding. Ghanbarpour and Akhtardanesh (2012) reported that Streptomycin showed a resistance of 11.90%, whereas in the present finding it is 100%. Deshpande (2005) reported sensitivity of Ceftriaxone to be 11.11% which is in close agreement with the present finding.

4.3.2 Haematobiochemical study:

It was reported that CEH-P complex affects certain blood constituents e.g. TLC, DLC, TEC, haemoglobin, BUN, creatinine, total protein, albumin, globulin and PCV etc. Thus in present investigation blood profile was studied to record the alterations therein.
Total Leucocyte Counts (TLC) :

The total leucocyte count was done on 0th, 5th and 10th day of the treatment in all the three groups and the mean values are presented in Table 4 and Fig 3.

Table 4. Total Leucocyte Count (×10³/µl) in different groups of bitches (Mean ±S.E.)

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>31.18±3.04^a</td>
<td>18.45±1.79^cd</td>
<td>10.56±0.06^cd</td>
<td>6.088</td>
<td>8.286</td>
</tr>
<tr>
<td>Group II</td>
<td>29.09±2.24^a</td>
<td>21.04±1.76^cd</td>
<td>14.59±1.06^cd</td>
<td>5.174</td>
<td>7.042</td>
</tr>
<tr>
<td>Group III</td>
<td>30.10±2.28</td>
<td>27.99±2.11^a</td>
<td>25.68±2.03^a</td>
<td>5.594</td>
<td>4.031</td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly

In group I, the mean leukocyte count on 0th day was 31.18±3.04×10³/µl. It reduced to 18.45±1.79×10³/µl and 10.56±0.06×10³/µl on 5th day and on 10th day respectively. In this group the values of 0th, 5th and 10th day significantly differ from each other.

In group II, the mean leukocyte count on 0th, 5th and 10th day were 29.09±2.24, 21.04±1.76 and 14.59±1.06. In this group, significant reduction was noticed from day 0th to day 5th and from day 5th to day 10th.

In group III, 30.10±2.28, 27.99±2.11 and 25.68±2.03 were the mean leukocyte count on 0th, 5th and 10th day. No significant reduction was noticed in this group.

The 0th day values between the three groups did not differ significantly. On 5th and 10th day, the values of group I and II differ significantly from that of group III, whereas the values between group I and II did not differ significantly.

The present finding is in close agreement with Jena et al. (2014a) and Jena et al. (2013a). Also the present values on 0th day are in agreement with those reported by Patil et al. (2013), Kaymaz et al. (1999), Emanuelli et al. (2012), Lakshmikanth et al. (2016) and Hagman et al. (2006b). However, lower values of TLC were
reported by Hagman et al. (2006a) 9.4±5.2 (×10³/µl), Hagman et al. (2009) 16.8±9.4 (×10³/µl), Mudasir et al. (2011) 22.22 ± 1.13 (× 10³/µl) and Ahamed et al. (2015) 15.11±3.02 (× 10³/µl). A contradictory higher levels of TLC, 64.367±11.03 (× 10³/µl) reported by Ravishankar et al. (2004).

The 10th day TLC values correlated with the findings of Gobello et al. (2003), Jena et al. (2013a) and Jena et al. (2014a). Gobello et al. (2003) showed on graph that the TLC values reduced to < 10000/mm³ after complete recovery from CEH-P. England et al. (2007) reported that haematological profiles of 21 of the bitches returned to normal within six days with Cloprostenol and Cabergoline treatment. This finding is in close agreement with the present finding.

Leucocytosis was observed in pre-treatment CEH-P bitches due to bacterial infection of uterus. The TLC values restored within physiological range on 10th day in group I and II indicating progressive recovery. A simultaneous improvement in health condition was also recorded. But in group III the values were still higher than normal values and improvement in general health condition was relatively slower than other groups. This clearly shows that increase in TLC is related to severity of the disease.

**Differential leucocyte count (DLC):**

The differential leucocyte count was done in all the three groups on 0th, 5th and 10th day.

**Neutrophil (%) :**

The mean values (group wise and day wise) for neutrophils are presented in Table 5 and Fig 4.
Table 5. Neutrophil (%) in different groups of bitches (Mean ±S.E.)

<table>
<thead>
<tr>
<th></th>
<th>0&lt;sup&gt;th&lt;/sup&gt; day</th>
<th>5&lt;sup&gt;th&lt;/sup&gt; day</th>
<th>10&lt;sup&gt;th&lt;/sup&gt; day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>80.78±1.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>72.71±0.92&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64.79±0.70&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.646</td>
<td>3.602</td>
</tr>
<tr>
<td>Group II</td>
<td>78.88±0.79&lt;sup&gt;a&lt;/sup&gt;</td>
<td>73.56±0.82&lt;sup&gt;b&lt;/sup&gt;</td>
<td>69.3±0.69&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.223</td>
<td>3.026</td>
</tr>
<tr>
<td>Group III</td>
<td>79.21±0.51&lt;sup&gt;a&lt;/sup&gt;</td>
<td>77.66±0.61&lt;sup&gt;b&lt;/sup&gt;</td>
<td>76.38±0.66&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.637</td>
<td>2.229</td>
</tr>
<tr>
<td>CD 5%</td>
<td>2.279</td>
<td>2.279</td>
<td>1.930</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td>3.101</td>
<td>1.930</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly

In group I, the mean neutrophil percentage on 0<sup>th</sup> day was 80.78±1.03%. After a significant reduction from 0<sup>th</sup> day, the value came to 72.71±0.92% on 5<sup>th</sup> day. A further reduction was noted to 64.79±0.70% on 10<sup>th</sup> day. The 10<sup>th</sup> day value was significantly different from both 0<sup>th</sup> and 5<sup>th</sup> day.

In group II, the mean neutrophil % on 0<sup>th</sup> day was 78.88±0.79%. It reduced significantly to 73.56±0.82% and 69.3±0.69% on 5<sup>th</sup> and 10<sup>th</sup> day, respectively. The 5<sup>th</sup> and 10<sup>th</sup> day values did not vary significantly.

In group III, the mean neutrophil % on 0<sup>th</sup> and 5<sup>th</sup> day were 79.21±0.51 and 77.66±0.61, respectively. No significant difference was noted between 0<sup>th</sup> and 5<sup>th</sup> day. However, the value on 10<sup>th</sup> day (76.38±0.66%) differed significantly from 0<sup>th</sup> and 5<sup>th</sup> day.

On 0<sup>th</sup> day, neutrophill percentage did not differ significantly between the groups. On 5<sup>th</sup> day values of group I and II showed significant difference from group III. However, the group I and II did not differ significantly from each other. The findings of 10<sup>th</sup> day between all the three groups differed significantly from each other.

The 0<sup>th</sup> day findings were similar to those of Ravishankar <i>et al.</i> (2004) 84.65±1.9%, Patil <i>et al.</i> (2013) 82.4±4.47%, Jena <i>et al.</i> (2013a) 78.28±2.37%, Jena <i>et al.</i> (2014a) 79.57±1.02% and Lakshmikanth <i>et al.</i> (2016) 84.00±2.43%. However, Mudasir <i>et al.</i> (2011), Mohan <i>et al.</i> (2015) and Ahmed <i>et al.</i> (2015) reported lower values of 72.0±0.54%, 73.35±1.58% and 66.6±1.06%.
Fig 3. Mean TLC ($\times 10^3/\mu l$) in different groups of bitches on different days

Fig 4. Mean Neutrophill(%) in different groups of bitches on different days
respectively. Ramsingh et al. (2013) found neutrophil > 90% in 2 bitches which is more than the present findings.

The 10th day findings were in accordance with Jena et al. (2013a) 65.71 ± 0.81% and Jena et al. (2014a) 69.86 ± 0.63%

An absolute neutrophilia was noticed in pre-treatment CEH-P bitches, which is the characteristic feature of bacterial infection. After treatment, the 10th day values of group I and II found within physiological range, but that of the group III was still higher than the upper limit of the physiological range.

**Lymphocyte (%):**

The mean values (group wise and day wise) for lymphocytes are presented in table 6 and Fig 5.

**Table 6. Lymphocyte (%) in different groups of bitches (Mean±S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>10.18±0.69c</td>
<td>18.76±0.63bA</td>
<td>27.31±0.56ab</td>
<td>1.862</td>
<td>2.534</td>
</tr>
<tr>
<td>Group II</td>
<td>11.57±0.71c</td>
<td>17.06±0.83bA</td>
<td>22.11±0.54ab</td>
<td>2.079</td>
<td>2.830</td>
</tr>
<tr>
<td>Group III</td>
<td>11.65±0.45bC</td>
<td>13.97±0.73ab</td>
<td>15.56±0.69ab</td>
<td>1.895</td>
<td>2.579</td>
</tr>
<tr>
<td>CD 5%</td>
<td>2.170</td>
<td>1.780</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td>2.954</td>
<td>2.423</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly

In group I, the mean lymphocyte percentage was 10.18±0.69%, 18.76±0.63% and 27.31±0.56% on 0th, 5th and 10th day, respectively. These values significantly differ from each other.

In group II, the mean lymphocyte percentage on 0th, 5th and 10th day were 11.57±0.71%, 17.06±0.83% and 22.11±0.54%, respectively. These values significantly differ from each other.
In group III, 11.65±0.45 was the mean lymphocyte percentage on 0\textsuperscript{th} day. The value increased significantly to 13.97±0.73\% and 15.56±0.69\% on 5\textsuperscript{th} and 10\textsuperscript{th} day. However, no significant difference was noted between 5\textsuperscript{th} and 10\textsuperscript{th} day.

The pre-treatment lymphocyte percentage was in accordance with 11.00±1.43\%, 10.08±1.13\% and 11.28±2.15\% reported by Jena \textit{et al.} (2013a), Mohan \textit{et al.} (2015) and Lakshmikanth \textit{et al.} (2016) respectively. Conversely, Ravishankar \textit{et al.} (2004) and Patil \textit{et al.} (2013) reported 13.43±1.75\% and 13.3±3.37\% higher levels of lymphocyte percentage.

Tenth day value correlates with findings of Jena \textit{et al.} (2013b) who reported 26.14 ± 0.86\% of lymphocyte after treatment with Cabergoline and Cloprostenol. Jena \textit{et al.} (2014a) reported 20.28 ± 0.42\% of lymphocyte after treatment with Cloprostenol.

Lymphocytopenia was noticed in CEH-P due to stress. Lymphocyte percentage was increased gradually during the treatment period in all the groups.

\textbf{Monocyte (\%)}:

The mean values (group wise and day wise) for monocytes are presented in Table 7 and Fig 6.

\textbf{Table 7. Monocyte (\%) in different groups of bitches (Mean ± S.E.)}

<table>
<thead>
<tr>
<th></th>
<th>0\textsuperscript{th} day</th>
<th>5\textsuperscript{th} day</th>
<th>10\textsuperscript{th} day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>6.87±0.42</td>
<td>5.96±0.48</td>
<td>5.36±0.52</td>
</tr>
<tr>
<td>Group II</td>
<td>7.13±0.30</td>
<td>6.68±0.36</td>
<td>6.25±0.32</td>
</tr>
<tr>
<td>Group III</td>
<td>6.75±0.21</td>
<td>6.66±0.26</td>
<td>6.63±0.25</td>
</tr>
</tbody>
</table>

In group I, the mean monocyte percentage was recorded as 6.87±0.42\% on 0\textsuperscript{th} day. On 5\textsuperscript{th} day and 10\textsuperscript{th} day, it reduced to 5.96±0.48\% and 5.36±0.52\%, respectively.

In group II, the mean monocyte percentage was 7.13±0.30 \% on 0\textsuperscript{th} day. It reduced to 6.68±0.36\% and 6.25±0.32\% on 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.
Fig 5. Mean Lymphocyte(%) in different groups of bitches on different days

Days

DAY 0  DAY 5  DAY 10

Lymphocyte (%)

GROUP I
GROUP II
GROUP III

Fig 6. Mean Monocyte(%) in different groups of bitches on different days

Days

DAY 0  DAY 5  DAY 10

Monocyte (%)

GROUP I
GROUP II
GROUP III
In group III, the mean monocyte percentage was 6.75±0.21%, 6.66±0.26% and 6.63±0.25% on 0th, 5th and 10th day.

Significant differences were noticed neither within nor between any groups.

The pre-treatment monocyte percentage is in accordance with Khan (2006) who reported it to vary from 5.91±0.49% to 7.12±0.88%. Higher value of 8.43±0.84% reported by Jena et al. (2013a). Lower values of 1.62±0.61%, 2.53±0.17%, 3.5±3.23% were reported by Ravishankar et al. (2004), Mudasir et al. (2011) and Patil et al. (2013).

The 10th day finding is in accordance with Jena et al. (2013a) who reported it to be 5.71 ± 0.28% after recovery from pyometra.

All the 0th day values are within the normal physiological range, but found towards the upper limit of the normal range. This indicates a mild monocytosis in CEH-P bitches.

**Eosinophil (%)**:

The mean values (group wise and day wise) for eosinophils are presented in table 8 and Fig 7.

**Table 8. Eosinophil (%) in different groups of bitches (Mean±S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group I</strong></td>
<td>2.47±0.13</td>
<td>2.63±0.13</td>
<td>2.77 ± 0.14^a</td>
</tr>
<tr>
<td><strong>Group II</strong></td>
<td>2.37±0.13</td>
<td>2.45±0.13</td>
<td>2.48 ± 0.13^ab</td>
</tr>
<tr>
<td><strong>Group III</strong></td>
<td>2.17±0.20</td>
<td>2.15±0.20</td>
<td>2.16 ± 0.18^a</td>
</tr>
<tr>
<td><strong>CD 5%</strong></td>
<td></td>
<td></td>
<td>0.455</td>
</tr>
</tbody>
</table>

Values bearing different superscripts in column differ significantly

In group I, the mean eosinophil percentage was 2.47±0.13%, 2.63±0.13% and 2.77±0.14% on 0th, 5th and 10th day, respectively.
In group II, the mean eosinophil percentage was 2.37±0.13%, 2.45±0.13% and 2.48±0.13% on 0\textsuperscript{th}, 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.

In group III, the mean eosinophil percentage was 2.17±0.20%, 2.15±0.20% and 2.16±0.18% on 0\textsuperscript{th}, 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.

There was no significant difference seen within any individual group on any days. The 0\textsuperscript{th} and 5\textsuperscript{th} day values were not significantly differ between the groups, but the values of 10\textsuperscript{th} day significantly differ between group I and III.

The 0\textsuperscript{th} day values are in close agreement with Jena \textit{et al.} (2013a) who reported 2.28±0.28% eosinophil in pyometra, but higher than 0.65±0.23%, 1.82±0.32% reported by Ravishankar \textit{et al.} (2004) and Lakshmikanth \textit{et al.} (2016), respectively. The 0\textsuperscript{th} day values were lower than 5.26 ± 0.17% reported by Mudasir \textit{et al.} (2011).

The 10\textsuperscript{th} day finding is in agreement with Jena \textit{et al.} (2013a) who reported it to be 2.43 ± 0.20% after recovery from pyometra.

Although all the 0\textsuperscript{th} day values were within the normal range, after treatment the values slightly increased in group I and II where as in group III the value slightly decreased.

**Total Erythrocyte Count (TEC):**

The Total erythrocyte counts were done in all three groups on 0\textsuperscript{th}, 5\textsuperscript{th} and 10\textsuperscript{th} day. The group wise and day wise mean values of TEC are presented in Table 9 and Fig 8.

**Table 9. Total Erythrocyte Count (×10\textsuperscript{6}/µl) in different group of bitches (Mean ± S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0\textsuperscript{th} day</th>
<th>5\textsuperscript{th} day</th>
<th>10\textsuperscript{th} day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>5.2±0.39</td>
<td>5.87±0.36</td>
<td>6.22±0.39</td>
</tr>
<tr>
<td>Group II</td>
<td>4.80±0.34</td>
<td>5.30±0.32</td>
<td>5.47±0.30</td>
</tr>
<tr>
<td>Group III</td>
<td>5.03±0.24</td>
<td>5.19±0.21</td>
<td>5.28±0.21</td>
</tr>
</tbody>
</table>
Fig 7. Mean Eosinophill(%) in different groups of bitches on different days

Fig 8. Mean TEC (×10⁶/μl) in different groups of bitches on different days
In group I, the mean TEC on 0\textsuperscript{th} day was 5.2±0.39(×10\textsuperscript{6}/µl). It non-significantly increased to 5.87±0.36(×10\textsuperscript{6}/µl) and 6.22±0.39(×10\textsuperscript{6}/µl) on 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.

In group II, the mean TEC on 0\textsuperscript{th} day was 4.80±0.34(×10\textsuperscript{6}/µl). It non-significantly increased to 5.30±0.32(×10\textsuperscript{6}/µl) and 5.47±0.30(×10\textsuperscript{6}/µl) on 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.

In group III, the mean TEC values were 5.03±0.24(×10\textsuperscript{6}/µl), 5.19±0.21(×10\textsuperscript{6}/µl) and 5.28±0.21(×10\textsuperscript{6}/µl) on 0\textsuperscript{th}, 5\textsuperscript{th} and 10\textsuperscript{th} day, respectively.

No significant difference was seen within any group. Likewise, no significant difference was seen between groups on any day.

The 0\textsuperscript{th} day findings are in accordance with values reported by Emanuelli et al. (2012)5.02±0.92 (×10\textsuperscript{6}/µl), Patil et al. (2013) 4.85±1.47(×10\textsuperscript{6}/µl), Kaymaz et al. (1999) 5.8±11.3(×10\textsuperscript{6}/µl), Anna et al. (2014) 5.58±1.44(×10\textsuperscript{6}/µl), Mohan et al. (2015) 4.70±0.20(×10\textsuperscript{6}/µl), Jena et al. (2013b) 5.48±0.17(×10\textsuperscript{6}/µl) and Ucmak et al. (2012)5.002 ± 0.426(×10\textsuperscript{6}/µl).

Patil et al. (2013) also found a non-significant increase of TEC from 4.85±1.47 to 6.31±0.94 after medicinal treatment. Similarly, Jena et al. (2013a) observed rise to 6.68 ± 0.17 from 5.51 ± 0.14 with treatment of cabergoline and cloprostenol the values are in accordance with the present findings. Ucmak et al. (2012) and Jena et al. (2013a) found a deterioration in TEC values even after antibiotics and supportive treatments. However, present findings showed a minor improvement in group III though the values are lesser than the group I and II.

In present investigation, drop in TEC was noticed in CEH-P bitches. The drop in TEC in CEH-P bitches might be due to decreased erythropoiesis as a result of toxic effects on the bone marrow and loss of erythrocytes to the uterus. In group I, the TEC values increase gradually to reach the normal range on 5\textsuperscript{th} day. Likewise, in group II the values on 10\textsuperscript{th} day were very close to the physiological range. But in group III, in spite of increased values, it could not reach the normal limits.
Haemoglobin (Hb):

The haemoglobin levels were estimated in all three groups on 0th, 5th and 10th day. The group wise and day wise mean values of haemoglobin are presented in Table 10 and Fig 9.

**Table 10. Haemoglobin (g %) in different groups of bitches (Mean ± S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>10.92±0.85</td>
<td>12.18±0.84</td>
<td>12.98±0.86</td>
</tr>
<tr>
<td>Group II</td>
<td>9.9±0.76</td>
<td>10.88±0.71</td>
<td>11.56±0.72</td>
</tr>
<tr>
<td>Group III</td>
<td>10.91±0.60</td>
<td>11.02±0.59</td>
<td>11.07±0.59</td>
</tr>
</tbody>
</table>

In group I, the mean haemoglobin on 0th day was 10.92 ± 0.85g%. The values increased non-significantly to 12.18±0.84g% and 12.98±0.86g% on 5th and 10th day, respectively.

In group II, the mean haemoglobin on 0th day was 9.9±0.76g%. It increased to 10.88±0.71g% and 11.56±0.72g% on 5th and 10th day, respectively. However, the differences between the days were not significant.

In group III, the mean haemoglobin on 0th, 5th and 10th day were 10.91±0.60g%, 11.02±0.59g% and 11.07±0.59g%, respectively. Differences between these values were insignificant.

No significant difference was noticed between the groups.

Similar pre-treatment observations were reported by Mudasir et al. (2011), Ucmak et al. (2012), Patil et al. (2013), Jena et al. (2013a), Sant’Anna et al. (2014) and Mohan et al. (2015). However, Hagman et al. (2006b), Lakshmikanth et al. (2016), Ahamed et al. (2015) and Emanuelli et al. (2012) reported higher levels of 11.7±2.5g%, 12.32±0.75g%, 13.66±0.58g% and 13.35±2.23g% respectively. Unlike the previous values, Kumari et al. (2012) reported a lower value of 8.95±0.37 g% of haemoglobin.
England et al. (2007) reported that all haematological values including haemoglobin found to be within normal range on day 6\(^{th}\) of Cloprostenol and Cabergoline treatment. This finding is in agreement the present finding of group I.

The pre-treatment haemoglobin levels were lower than normal value. It is due to decreased production and increased loss of RBCs in CEH-P. In group I, the value laid within physiological range on day 5\(^{th}\). In group II, the values on day 10\(^{th}\) were very closer to the physiological range, whereas a little improvement was noticed in group III and could not reach upto the normal range.

**Packed Cell Volume (PCV):**

The blood urea nitrogen levels were estimated in all three groups on 0\(^{th}\), 5\(^{th}\) and 10\(^{th}\) day. The group wise and day wise mean values of BUN are presented in Table 11 and Fig 10.

**Table 11. Packed Cell Volume (%) in different groups of bitches (Mean±S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0(^{th}) day</th>
<th>5(^{th}) day</th>
<th>10(^{th}) day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>35.22±0.98(^b)</td>
<td>37.75±0.92(^ab)</td>
<td>40.28±0.96(^a)</td>
<td>2.820</td>
<td>3.839</td>
</tr>
<tr>
<td>Group II</td>
<td>35.54±0.70</td>
<td>36.74±0.70</td>
<td>37.72±0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>33.47±0.80</td>
<td>33.53±0.79</td>
<td>33.68±0.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 5%</td>
<td>2.385</td>
<td>2.414</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td>3.245</td>
<td>3.285</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly

In group I, the mean PCV on 0\(^{th}\) day was 35.22±0.98\(^b\). It reduced to 37.75±0.92\(^ab\) and 40.28±0.96\(^a\) on 5\(^{th}\) and 10\(^{th}\) day, respectively. A significant difference was observed between 10\(^{th}\) and 0\(^{th}\) day, whereas the 5\(^{th}\) day value was statistically not differed from either of 0\(^{th}\) and 10\(^{th}\) day.

In group II, the mean PCV were 35.54±0.70\(^b\), 36.74±0.70\(^b\) and 37.72±0.69\(^b\) on 0\(^{th}\), 5\(^{th}\) and 10\(^{th}\) day, respectively. No significant difference was observed between the days.
Fig 9. Mean Haemoglobin (g%) in different groups of bitches on different days

Fig 10. Mean PCV (%) in different groups of bitches on different days
In group III, the mean PCV were 33.47±0.80%, 33.53±0.79% and 33.68±0.77% on 0th, 5th and 10th day, respectively. These values did not differ statistically to each other.

On 0th day, statistical difference was not found between groups. On 5th day, group I and II values were statistically different from group III. However, no statistical difference was noticed between group I and II.

The present finding of PCV was in agreement with Jena et al. (2013a) and Jena et al. (2014a).

The 0th day findings are in close agreement with the findings of Ravishankar et al. (2004), Ucmak et al. (2012), and Lakshmikanth et al. (2016). Higher levels of 49±13 % reported by Kaymaz et al. (1999), whereas Lower values of 29.73±8.48 % reported by Patil et al. (2013).

England et al. (2007) observed that with Cloprostenol and Cabergoline treatment, all haematological abnormalities including haematocrit value were resolved within 6 days. This finding is in close agreement with finding of group I.

The PCV values decreased in CEH-P bitches. It gradually increased with treatment given. The values increased and found within normal range on 5th day in group I and on 10th day in group II, whereas it was still lower than normal value in group III on 10th day.

**Blood urea nitrogen (BUN):**

The blood urea nitrogen levels were estimated in all three groups on 0th, 5th and 10th day. The group wise and day wise mean values of BUN are presented in Table 12 and Fig 11.
Table 12. Blood urea nitrogen (BUN) levels (mg/dl) in different groups of bitches (Mean ± S.E.)

<table>
<thead>
<tr>
<th></th>
<th>0&quot; day</th>
<th>5&quot; day</th>
<th>10&quot; day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>22.82±1.47(_a)</td>
<td>16.14±1.14(_b)</td>
<td>12.71±0.83(_b)</td>
<td>3.7575</td>
<td>5.114</td>
</tr>
<tr>
<td>Group II</td>
<td>22.55±1.14(_a)</td>
<td>18.0±0.98(_b)</td>
<td>15.04±0.86(_b)</td>
<td>2.957</td>
<td>4.025</td>
</tr>
<tr>
<td>Group III</td>
<td>22.10±1.32</td>
<td>20.95±1.28(_a)</td>
<td>19.74±1.31(_a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 5%</td>
<td></td>
<td>3.651</td>
<td>3.022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td></td>
<td>4.113</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly.

In group I, the mean BUN value was 22.82±1.47 mg/dl on 0\(^{th}\) day. It decreased to 16.14±1.14mg/dl and 12.71±0.83mg/dl on 5\(^{th}\) and 10\(^{th}\) day, respectively. The values on all the three days differed significantly to each other.

In group II, the mean BUN value was 22.55±1.14mg/dl on 0\(^{th}\) day. It declined to 18.0±0.98mg/dl and 15.04±0.86mg/dl on 5\(^{th}\) and 10\(^{th}\) day, respectively. The values on all the three days differed significantly to each other.

In group III, the mean BUN value was 22.10±1.32 mg/dl on 0\(^{th}\) day. It significantly reduced to 20.95±1.28mg/dl and 19.74±1.31mg/dl on day 5\(^{th}\) and 10\(^{th}\), respectively. The values on 5\(^{th}\) and 10\(^{th}\) day did not differ significantly.

On 0\(^{th}\) day, the mean BUN values did not differ significantly between the groups. On 5\(^{th}\) day, a significant difference was noticed between group I and III. However, group II was statistically in different to group I and II. On 10\(^{th}\) day, both group I and II differed significantly from group III, but there was no significant difference between group I and II BUN values.

Similar pre-treatment BUN values were recorded by Jena \textit{et al.} (2013b) 23.43±1.17 mg/dl and Ahamed \textit{et al.} (2015) 19.88±4.91mg/dl. Bigliardi \textit{et al.} (2004) also found BUN within normal range in CEH-P bitches. Contradictory to the present findings are reported by Ravishankar \textit{et al.} (2004), Mudasir \textit{et al.} (2011), Gupta \textit{et al.} (2013b) and Patil \textit{et al.} (2013) recorded a higher BUN levels of 59.98±8.19 mg/dl, 31.04±0.73 mg/dl, 60.78±10.03 mg/dl and 36.45±22.86
mg/dl respectively. Hagman et al. (2006a) and Hagman et al. (2009) reported the BUN concentration of 4.6±1.8 mmol l⁻¹ and 5.0±3.2 mmol l⁻¹ which is equivalent to 12.88±5.04 mg/dl and 14±8.96 mg/dl respectively. These values are lower than the present findings.

BUN values increases in CEH-P bitches due to organic tissue destruction and dehydration. However, comparatively less severe cases the BUN levels in serum does not exceed normal range as dehydration was not severe to cause pre-renal azotaemia. In the present investigation, the pre-treatment values of BUN were within the normal range, but are close to the upper limit of normal range (8-25mg/dl). The values gradually declined with treatment on 5th and 10th day. These findings suggest that there is a mild rise in BUN levels in bitches with CEH-P.

**Creatinine :**

Serum creatinine levels of experimental bitches were estimated on 0th, 5th and 10th day. The mean values are presented in Table 13 and Fig 12.

**Table13. Creatinine levels (mg/dl) in different groups of bitches (Mean ± S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>1.41±0.10ᵃ</td>
<td>0.96±0.89ᵇ</td>
<td>0.67±0.04ᶜ</td>
<td>0.249</td>
<td>0.339</td>
</tr>
<tr>
<td>Group II</td>
<td>1.32±0.08ᵃ</td>
<td>1.05±0.07ᶜ</td>
<td>0.88±0.09ᵈ</td>
<td>0.250</td>
<td>0.340</td>
</tr>
<tr>
<td>Group III</td>
<td>1.33±0.09</td>
<td>1.22±0.09</td>
<td>1.16±0.09ᵃ</td>
<td>0.240</td>
<td></td>
</tr>
<tr>
<td>CD 5%</td>
<td></td>
<td></td>
<td></td>
<td>0.240</td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td></td>
<td></td>
<td></td>
<td>0.327</td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly

In group I, the creatinine concentration was 1.41±0.10 mg/dl on 0th day. It significantly decline to 0.96±0.89 mg/dl and 0.67±0.04 mg/dl on 5th and 10th day, respectively. The creatinine values on these three days differed significantly to each other.
Fig 11. Mean BUN (mg/dl) in different groups of bitches on different days

Fig 12. Mean Creatinine (mg/dl) in different groups of bitches on different days
In group II, the creatinine concentration was 1.32±0.08 mg/dl on 0th day. It decreased significantly to 1.05±0.07 mg/dl and 0.88±0.09 mg/dl on 5th and 10th day, respectively. However, difference was not significant between 5th and 10th day.

In group III, the creatinine concentration was 1.33±0.09 mg/dl, 1.22±0.09 mg/dl and 1.16±0.09 mg/dl on 0th, 5th and 10th day. No significant reduction was noticed between the days.

No significant difference was found between groups on 0th and 5th day. On 10th day, both group I and II differed significantly from group III, but there was no significant difference between group I and II creatinine values.

The pre-treatment observations on creatinine concentrations were parallel to observations of Ravishankar et al. (2004) and Lakshmikanth et al. (2016) who reported the creatinine values of 1.35±0.13 mg/dl and 1.40±0.23 mg/dl respectively. However, Mudasir et al. (2011), Jena et al. (2013a) and Ahmed et al. (2015) reported higher creatinine concentrations of 3.37±0.08 mg/dl, 2.20±0.08 mg/dl and 2.4±0.52 mg/dl. Contrary to these findings, Hagman (2006a) and Hagman (2009) reported a creatinine concentration of 71±31 (mmol l⁻¹) and 81±22 (mmol l⁻¹) which are equivalent to 0.86±0.34 mg/dl and 0.89±0.24 mg/dl. These values are much lower than the present finding.

The post-treatment values were in close agreement with Khan (2006) who reported it to be 0.41±0.07 mg/dl after recovery from pyometra.

Renal dysfunction has been mentioned as a feature of canine pyometra. However, creatinine concentrations are not usually elevated, unless pre-renal azotemia develops as a consequence of dehydration. The creatinine concentrations on 0th day were found within physiological range, but close to the upper limit. It gradually decline as improvement seen with treatment.

**Total protein :**

Serum total protein levels of experimental bitches were estimated on 0th, 5th and 10th day. The mean values are presented in Table 14 and Fig 13.
Table 14. Total protein levels (g/dl) in different groups of bitches (Mean ± S.E.)

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>8.11±0.24a</td>
<td>6.98±0.20b</td>
<td>6.34±0.19c</td>
<td>0.636</td>
<td>0.866</td>
</tr>
<tr>
<td>Group II</td>
<td>7.90±0.22a</td>
<td>7.12±0.21b</td>
<td>6.67±0.20b</td>
<td>0.628</td>
<td>0.855</td>
</tr>
<tr>
<td>Group III</td>
<td>7.41±0.34</td>
<td>7.14±0.28</td>
<td>7.07±0.27</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row differ significantly.

In group I, the mean total protein on 0th day was 8.11±0.24g/dl. It reduced significantly to 6.98±0.20g/dl and 6.34±0.19g/dl on 5th and 10th day, respectively. Here, all the three values significantly different to each other.

In group II, the mean total protein on 0th day was 7.90±0.22g/dl. It reduced significantly to 7.12±0.21g/dl and 6.67±0.20g/dl on 5th and 10th day, respectively. However, significant difference was not noticed between 5th and 10th day.

In group III, the mean total proteins were 7.41±0.34g/dl, 7.14±0.28g/dl and 7.07±0.27g/dl on 0th, 5th and 10th day respectively. These values were statistically indifferent.

No significant difference was observed between any of the three groups on any day.

In the present study, the 0th day findings were in tune with findings of Kaymaz et al. (1999), Hagman (2004), Hagman et al. (2006a), Hagman et al. (2006b), Ucmak et al. (2012), Gupta et al. (2013b), Jena et al. (2013a) and Lakshmikanth et al. (2016). Higher values of 9.34±1.08g/dl and 9.0g/dl were reported by Emanuelli et al. (2012) and Sant’Anna et al. (2014). Lower value of 4.78±0.89 g/dl was observed by Patil et al. (2013).

The post-treatment values were in accordance with Jena et al. (2013a) Jena (2014a) et al. and Patil et al. (2013).
The pre-treatment total protein values were towards the upper limit of physiological range or slightly higher. This indicates a mild hyperproeinaemia in CEH-P bitches. The increase in protein level could have contributed by elevated globulin fraction or due to dehydration. The values gradually decrease on 5th and 10th day as treatment advances.

**Albumin:**

Serum albumin levels of experimental bitches were estimated on 0th, 5th and 10th day. The mean values are presented in Table 15 and Fig 14.

**Table 15. Albumin levels (g/dl) in different groups of bitches (Mean±S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>2.2±0.12</td>
<td>2.45±0.15</td>
<td>2.58±0.18A</td>
</tr>
<tr>
<td>Group II</td>
<td>2.03±0.10</td>
<td>2.17±0.10</td>
<td>2.22±0.11AB</td>
</tr>
<tr>
<td>Group III</td>
<td>2.05±0.08</td>
<td>2.05±0.08</td>
<td>2.01±0.07B</td>
</tr>
<tr>
<td>CD 5%</td>
<td></td>
<td></td>
<td>0.389</td>
</tr>
</tbody>
</table>

Values bearing different superscripts in column differ significantly

In group I, the mean albumin value was 2.2±0.12g/dl on 0th day. It decreased to 2.45±0.15g/dl and 2.58±0.18g/dl on 5th and 10th day, respectively.

In group II, the mean albumin value was 2.03±0.10. It insignificantly decreased to 2.17±0.10g/dl and 2.22±0.11g/dl on 5th and 10th day, respectively.

In group III, the mean albumin values were 2.05±0.08g/dl, 2.05±0.08g/dl and 2.01±0.07g/dl on 0th, 5th and 10th day respectively.

Significant difference was not found within any group. Likewise, no significant difference was noticed between groups on 0th and 5th day. However, a significant difference was noticed on day 10 between group I and III, while the group II was significantly indifferent to both 0th and 10th day values.

The day 0th values of the present findings were in close agreement with findings of Ravishankar et. al. (2004), Hagman et al. (2009), Gupta et al.
Fig 13. Mean Total Protein (g/dl) in different groups of bitches on different days.

Fig 14. Mean Albumin (g/dl) in different groups of bitches on different days.
(2013b), Patil et al. (2013) and Lakshmikanth et al. (2016). Sant'Anna et al. (2014) also found albumin concentration within a range of 1.9 to 2.2 g/dl, which is in tune with the present finding. Higher values were reported by Hagman (2004) 3.1 ± 0.3 g/dl and Jena et al. (2013b) 2.84 ± 0.22 g/dl.

The pre-treatment observations showed hypoalbuminemia in all the groups. These alterations might be due to loss of albumin via the damaged kidneys and/or increased production of globulin as a defense mechanism against infection. The albumin concentration gradually increase with treatment. In group I, the hypoalbuminemia resolved and laid within normal range on 5th day. In group II, the albumin concentration was very close to normal range on 10th day. But in group III, the hypoalbuminemia did not resolved.

**Globulin:**

The mean globulin levels of experimental bitches were estimated on 0th, 5th and 10th day. The mean values are presented in Table 16 and Fig 15.

**Table 16. Globulin levels (g/dl) in different groups of bitches (Mean ± S.E.)**

<table>
<thead>
<tr>
<th></th>
<th>0th day</th>
<th>5th day</th>
<th>10th day</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>5.91±0.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.53±0.21&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3.78±0.20&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.645</td>
<td>0.878</td>
</tr>
<tr>
<td>Group II</td>
<td>5.87±0.32&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.96±0.25&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>4.51±0.25&lt;sup&gt;bcd&lt;/sup&gt;</td>
<td>0.763</td>
<td>1.039</td>
</tr>
<tr>
<td>Group III</td>
<td>5.36±0.32</td>
<td>5.28±.31</td>
<td>5.24±0.29&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 5%</td>
<td></td>
<td></td>
<td></td>
<td>0.755</td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td></td>
<td></td>
<td></td>
<td>1.027</td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly.

In group I, the mean globulin concentration was 5.91±0.23g/dl on 0th day. It significantly decreased to 4.53±0.21g/dl and 3.78±0.20g/dl on 5th day and 10th day, respectively. All the three values were significantly differed from each other.

In group II, the mean globulin concentration was 5.87±0.32g/dl on 0th day. It reduced significantly to 4.96±0.25g/dl and 4.51±0.25g/dl on 5th and 10th day. However, the 5th and 10th day values did not differ significantly.
In group III, the mean globulin concentration were 5.36±0.32g/dl, 5.28±0.31g/dl and 5.24±0.29g/dl on 0th, 5th and 10th day. These values did not differ significantly to each other.

On 0th and 5th day, no significant difference was noticed among the three groups. On 10th day, significant difference was noticed between group I and III, while group II value was statistically similar to both group I and III.

The pre-treatment values were similar to 5.80±0.37 g/dl, 5.29±0.41g/dl and 5.21±0.31g/dl reported by Ravishankar et al. (2004), Gupta et al. (2013b) and Jena et al. (2013a) respectively. However, Lakshmikanth et al. (2016) reported 4.94±0.32g/dl which is lesser than the present findings.

The post-treatment values were in close agreement with Jena et al. (2013a) 3.23±0.03g/dl and Jena et al. (2014a) 3.17±0.04g/dl.

Globulin values were found towards the upper limit of normal range to slightly higher than normal. It suggests mild hyperglobulinemia in CEH-P. This might be due to increased antigenic stimulation. These values gradually dropped with due course of treatment.

**Progesterone:**

The mean serum progesterone levels of experimental bitches were estimated on 0th, 5th and 10th day. The mean values are presented in Table 17 and Fig 16.

<table>
<thead>
<tr>
<th>Group</th>
<th>0th day (Mean±S.E.)</th>
<th>5th day (Mean±S.E.)</th>
<th>10th day (Mean±S.E.)</th>
<th>CD 5%</th>
<th>CD 1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>9.25±3.19&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.26±0.30&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.58±0.10&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>5.454</td>
<td>7.423</td>
</tr>
<tr>
<td>Group II</td>
<td>8.24±2.66&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.55±0.50&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.77±0.18&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>4.617</td>
<td>6.284</td>
</tr>
<tr>
<td>Group III</td>
<td>10.53±3.34</td>
<td>11.32±3.46&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.64±4.00&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD 1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values bearing different superscripts in row and column differ significantly.
Fig 15. Mean Globulin (g/dl) in different groups of bitches on different days

Fig 16. Mean Progesterone (ng/ml) in different groups of bitches on different days
In group I, the mean serum progesterone concentration was 9.25±3.19 on 0th day. It decreased significantly to 1.26±0.30 ng/ml and 0.58±0.10 ng/ml on 5th and 10th day, whereas no significant difference was noticed between 5th and 10th day values.

In group II, the mean serum progesterone concentration was 8.24±2.66ng/ml on 0th day. It decreased significantly to 1.55±0.50ng/ml and 0.77±0.18 ng/ml on 5th and 10th day. No significant difference was noticed between 5th and 10th day values.

In group III, the mean serum progesterone concentrations were 10.53±3.34ng/ml, 11.32±3.46ng/ml and 13.64±4.00ng/ml on 0th, 5th and 10th day, respectively. No significant difference was noticed between the days.

On 0th day, the progesterone concentration did not vary statistically between groups. But on 5th and 10th day, both group I and II differed significantly from group III, but there was no significant difference between group I and II.

The 0th day findings are in accordance with Gupta et al. (2013) who reported it to be 11.20±2.88 ng/ml in pyometric bitches. Bigliardi (2004) and Batista (2015) reported serum progesterone to vary between 2 to 25ng/ml, which correlates with the present findings whereas Domoslawska et al. (2010) reported in 34.47±9.54 ng/mL, which value is higher than the present finding.

The post-treatment observations were in agreement with England et al. (2007) and Krekeler (2010). England et al. (2007) reported that > 2.0 ng/ml was found in 15 out of 19 bitches and by day 6th, it was less than 1·0 ng/ml in all of the bitches with the treatment of cloprostenol and cabergoline. Krekeler (2010) reported that if prostaglandins are used for treatment of canine pyometra, reduction in serum progesterone level will be within 48 hours, which are found similar as in the present investigation.

In group I and II, the concentration declined, might be due to luteolysis enabled by Cloprostenol and Cabergoline. However, it continued to increase in group III, might be due to persistent CL.
4.4 Post-Treatment Recovery Status

The post treatment recovery status of group I, II and III are presented in Table 18 and Fig 17.

Table 18. Post-Treatment Recovery Status

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of bitches Treated</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>No. of Recovered bitches</td>
<td>8</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Recovery rate (%)</td>
<td>100</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>No. of bitches shown estrous</td>
<td>7</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>No. of bitches mated</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>No. of bitches conceived</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Conception Rate (%)</td>
<td>66.66</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>No. of bitches recurred</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Recurrence rate (%)</td>
<td>25</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Group I: Cloprostenol + Cabergoline + Antibiotic

Eight bitches in this group were treated with cloprostenol, cabergoline and antibiotics as indicated by AST. All the eight treated bitches were cured completely. Their hemato-biochemical values come to normal range on day 10th. Thus efficacy of treatment was 100%. Seven out of the eight animals came to estrus. Out of the seven, six were bred and four conceived after breeding. So, the conception rate was 66.66%. Recurrence was noticed in 2 bitches (66.66%) that were subjected to ovariohysterectomy.

The present finding of recovery rate was in agreement with England et al. (2007) and Jena et al. (2013a) who showed recovery rate of 95.45% and 100%. Corrada et al. (2006) reported a recovery rate of 92.85% and 73.33% in cases of pyometra and endometritis. The present finding of conception rate was higher
than Corrada et al. (2006) and England et al. (2007) who reported that 50% and 33.33%, but less than 71.43% reported by Jena et al. (2013a). Corrada et al. (2006), England et al. (2007) and Jena et al. (2013a) showed a recurrence rate of 20.68%, 19.04% and 28.57% which values were in accordance with the current observation. England et al. (2007) reported a normal blood haematological profile and normal serum biochemistry in all the treated bitches affected with pyometra after completion of treatment using a combination of Cloprostenol and Cabergoline.

**Group II : Cloprostenol + Antibiotics**

In this group, eight bitches were treated with Cloprostenol along with antibiotics and supportive therapy. Antibiotics were used as indicated by individual case based on AST. All the eight treated cases were cured indicating 100% recovery rate. The conception rate and recurrence rate were recorded as 50% each. Recurred animals subjected to ovariohysterectomy.

The finding of recovery rate in present study is similar to that of Jena et al. (2014a) and Gobello et al. (2003) who reported it 100%. However, Fieni (2006) and Khan et al. (2007) reported 84.4% and 83.33% recovery rates after using cloprostenol which is lower than the present study. Recurrence rate is lower than 85.72% reported by Jena et al. (2014a), whereas higher than 26.66% reported by Gobello et al. (2003). Conception rate is found to be higher than 14.28% reported by Jena et al. (2014a). As Kumari et al. (2011) found treatment with low dose of Cloprostenol and the use of antibiotics was a safe and effective treatment for open pyometra.

**Group III : Antibiotics**

In this group, Eight bitches were treated with antibiotics and supportive therapy only. Recovery rate, conception rate and recurrence rate were recorded as 25%, 0% and 100% respectively. Six animals did not recovered within seven days of treatment. The non-recovered animals were subjected to ovariohysterectomy.

Finding of the present study is correlated with Fukuda (2001), Ucmak et al. (2012), Jena et al. (2014a) and Mahesh et al. (2014) who reported that use of IV infusion, antibiotics and other supportive therapies were not effective in bitches
with pyometra. However, Singh *et al.* (2008) and Singh *et al.* (2010) reported complete recovery from pyometra within 6 days after using antibiotics and supportive therapy.

4.5 Observations on side effects of Cloprostenol:

Observations on side effects of Cloprostenol treatment were recorded in group I and II. The results thereof are presented in Table 19 and Fig 18.

**Table 19. Observation on side effects of Cloprostenol**

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of bitches shown side effect</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>Vomition</td>
<td>1</td>
<td>12.5</td>
</tr>
<tr>
<td>Salivation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urination</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Defecation</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>Restlessness</td>
<td>5</td>
<td>62.5</td>
</tr>
<tr>
<td>Hyperpnoea</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Depression</td>
<td>2</td>
<td>25</td>
</tr>
</tbody>
</table>

In both group I and II, the percentage of animal showing vomition were 12.5%, salivation 0%, urination 0% and defecation 25%. Percentage of various side effects in group I and II were restlessness (62.5% and 50%), hyperpnoea (50% and 62.5%) and depression (25% and 37.5%), respectively. No side effects were observed in four animals (One from group I and 3 from group II) i.e. in 25% of animals.
Fig 17. Post-Treatment Recovery Status in different groups of bitches

- Recovery rate (%)
- Conception Rate (%)
- Recurrence rate (%)

Fig 18. Side effects (%) of Cloprostenol in different groups of bitches

Group I
Group II
Fieni (2006) found vomition affected 18.18% of animal which is in close agreement with the present finding. A higher percentage of vomition (42.86%-57.14%) and restlessness (42.86%-57.14%) was reported by Jena et al. (2013a). Similar to present finding Jena et al. (2013a) did not observe salivation. Fieni (2006) reported a higher proportion i.e. 45.5% animal did not show any side effects. Contrary to the present study, Gobello et al. (2003) and Meter and Wright (2000) reported no side effects on cloprostenol administration in bitches with the dose rate of 1µg/kg b. wt.

In the present investigation, restlessness and hyperpnoea were the common side effects. The side effects started within 5-10 min of Cloprostenol administration and persists for 20-45min. The incidence of adverse effects was reduced after each successive dose of prostaglandin in the present study. Four animals, defecated within 30min of Cloprostenol administration. But diarrhoea was not observed in any of them and treatment was not required for this.

Food and water were withheld 4-6 hour prior and 1 hour after Cloprostenol administration. Metoclopramide was given 15 min prior to Cloprostenol administration. So vomition was not observed in most of the cases. However, in 2 cases mild vomition was observed. Salivation were absent in all animals. It is because administration of atropine sulphate 10-15 min prior to cloprostenol. Inj. Cloprostenol was diluted with equal amount of normal saline before each administration. After giving Cloprostenol animals were given walk to facilitate early metabolism to reduce its side effects.
SUMMARY

CEH-P complex is a most commonly observed reproductive disorder in the middle-aged bitches. The condition affects fertility and sometimes it proves to be life threatening. At present ovariohysterectomy is the treatment of choice. However, it is associated with risk of anaesthesia, risk of development of peritonitis and stump pyometra. Moreover, it does not help in toxaemic cases and when fertility of animal is required to be conserved. Thus, some medical therapy is needed as an alternative to ovariohysterectomy. Therefore, the present study was undertaken to assess the efficacy of certain medical therapies in the treatment of canine pyometra.

In the present investigation, 24 CEH-P bitches were included. The bitches were diagnosed on the basis of history, symptoms, clinical examination and ultrasonography. The observed signs and symptoms include vaginal discharge, anorexia, polyuria, polydipsia, vomition, fever, hyperpnoea, hyeremic mucus membrane, dehydration, and lethargy etc.

The 24 bitches were randomly divided into 3 groups (each comprising of 8 bitches) and subjected to one of the following treatment regimens.

Group I : Cloprostenol + Cabergoline + Antibiotics

Group II : Cloprostenol + Antibiotics

Group III : Antibiotics

The initial antibiotic treatment was with amoxicillin/clavulanic acid till the result of Antibiotic Sensitivity obtained. Afterwards antibiotics were given as per the sensitivity results in individual animals. As per the result of AST amoxicillin/clavulanic acid was found to be the best, followed by ampicillin/ sulbactam and chloramphenicol.

The hematobiochemical studies revealed that total leucocyte count, neutrophil percentage, monocyte percentage, total protein, globulin and blood urea nitrogen levels were found to be higher in all bitches of CEH-P complex, whereas lymphocyte percentage, total erythrocyte count, haemoglobin, packed cell volume and albumin were reduced. In response to the treatment, the values
found within the normal range on day 10th in bitches except those were in the control group. However, Creatinine and Eosinophil percentage were found to be within the physiological range during pretreatment and post treatment period in CEH-P bitches.

The ultrasonographic findings indicated that a uterine diameters became greater with accumulation of fluid inside the lumen along with endometrial thickening was observed in CEH-P bitches. The diameter gradually decrease with treatment and found to be <1cm in group I and II which value in considered to be normal, while in control group it was still >1cm. The earlier decrease in uterine diameter in group I and II may be the result of early evacuation of uterine content, facilitated by cloprostenol and cabergoline.

The progesterone concentration in bitches did not show any particular pattern in CEH-P bitches. It varied from 2 to 25 ng/ml. In both group I and II, its concentration decrease gradually which may be due to regression of corpus luteum, the source of progesterone. But in group III, its concentration was continued to increase except two animals who recovered.

As regard the recovery rate of treatment regimens is concerned, both group I (Cloprostenol.+ Cabergoline + Antibiotics) and II (Cloprostenol + Antibiotics ) showed 100% efficacy on day 10th. In group III, recovery percentage was less (25%) and non-recovered animals were subjected to ovariohysterectomy.

Among the recovered animals, the conception rates were 66.66%, 50% and 0% whereas the recurrence rates were found to be 25%, 50% and 100% in group I, II and III respectively. All the eight recurred bitches were subjected to ovariohysterectomy.

The efficacy of individual treatment regimen was decided on the basis of recovery rate, recurrence rate and conception rate. Again, the recovery rate was assessed by reduction in uterine diameter, improvement of general condition, cessation of vaginal discharge, disappearance of all other clinical signs and symptoms and returning of normal hematobiochemical values.

Among all the treatment regimens, group I i.e. cloprostenol + cabergoline + antibiotic was found to be most effective treatment in cases of CEH-P complex
in the bitches. Side effects of cloprostenol were observed in group I and II bitches. Restlessness and hyperpnoea were noticed as the most common side effects. Others were defecation, vomition and depression.

**CONCLUSION**

In the light of present study, it is concluded that,

1. Ultrasonography is tremendously valuable in diagnosis of CEH-P complex, as it can able to show the endometrial thickening and fluid accumulation inside the uterus. It also help to take follow up in CEH-P cases as based on measurement of the uterine diameter.
2. Leukogram may be used as a diagnostic aid in CEH-P complex as invariably there is leucocytosis accompanied with neutrophillia.
3. Biochemical values does not show any distinctive changes in CEH-P. However, it shows mild hyperproteinaemia and hyperglobinemia.
4. The low doses of cloprostenol, a synthetic prostaglandin in conjunction with cabergoline and antibiotics appears to be superior treatment regimen, because it results in expulsion of the uterine exudates. It can be also causes reduction in serum progesterone level which helps to reduce the thickness of endometrium.
5. Broad spectrum antibiotic along with supportive therapy may resolve pyometra, provided it is instituted at an early stage following Antibiotic Sensitivity Test. However, it may associate with a high recurrence rate.


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VITA

The author Dr. Jagyaseni Meher was born on 5th December 1991 at Mukhiguda, Dist-Kalahandi, Odisha. She has passed her Secondary education from Police High School, Reserve Police Line, Bhawanipatna in the year 2007 and Higher Secondary education from Vedbyash Residential College, Saradhabali in the year 2009.

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She is life member of ISSAR (Indian Society for Study of Animal Reproduction).

She presented an oral presentation on “Management of Repeat Breeding in Bitches” in XIV Annual Conference of Indian Association of Women Veterinarians (IAWV) and National Seminar on Recent Advances in Veterinary and Animal Sciences and Role of Women Veterinarian held at Krantisinh Nana Patil College of Veterinary Science, Shirwal from 8th to 10th October 2015.

Her abstract on “Therapeutic Management of Cystic Endometrial Hyperplasia Pyometra complex” was published in the compendium of XXXI Annual Convention of ISSAR held at Veterinary College, Hebbal, Bangalore during 3rd to 5th December 2015.

Author also have ‘B’ certificate in the Combined annual Training Camp of National Cadet Crops at Unit I (0) R &V SQN, NCC, Bhubaneswar.

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She joined guide during her schooling and actively participated in social works. She actively participated in cultural activities during her School and College life. She also took part in vaccination camps and health camps during her undergraduate and postgraduate studies.
ABSTRACT

The present study entitled "Cloprostenol and Cabergoline Therapy in Cystic Endometrial Hyperplasia – Pyometra Complex in Bitches" was undertaken in the Department of Animal Reproduction, Gynaecology and Obstetrics, Nagpur Veterinary College, Nagpur. Main objective of the study was to come out with
suitable medicinal treatment as an alternative to surgical treatment (Ovariohysterectomy) on CEH-P complex.

A total of twenty four bitches were selected on the basis of history, symptoms, clinical examination and ultrasonographic findings, which were divided into 3 equal groups. Group I was treated with cloprostenol, cabergoline, antibiotics and supportive therapy. Group II was treated with cloprostenol, antibiotics and supportive therapy. Group III was treated with antibiotics and supportive therapy only. Antibiotics were used as per the sensitivity results.

Hematobiochemical examinations were undertaken on day 0, 5th and 10th to support the diagnosis and assess the efficacy of treatment regimens chosen for present study. Leukocytosis along with neutrophilia was the most distinctive hematological change. TEC and haemoglobin were found to be decreased. Concerning biochemical changes, hyperprotenaemia and hyperglobinaemia were seen, though degrees were not higher.

By ultrasonography, the uterine status was figured out and uterine diameter was measured on day 0, 5th and 10th. As per the result of AST amoxicillin/ clavulanic acid was found to be the best, followed by ampicillin / sulbactam and chloramphenicol.

The efficacy of individual treatment regimen was decided on the basis of recovery rate, recurrence rate and conception rate. Likewise, the recovery rate was assessed by reduction in uterine diameter, improvement of general condition, cessation of vaginal discharge, disappearance of all other clinical signs and symptoms and returning of normal hematobiochemical values.

Reduction of uterine diameter, disappearance of clinical signs and improvement of general condition and returning of normal hematobiochemical values were faster in group I than group II whereas group III was found to be the slowest.
Recovery rate, conception rate and recurrence rate were 100%, 66.66% and 25% in group I, whereas in group II 100%, 50% and 50% respectively and group III was found to be the poorest such as 25%, 0% and 100% respectively.

It can be concluded that considering the recovery, conception and recurrence rate, combination therapy i.e. cloprostenol with cabergolin followed by fluid therapy was found to be effective for CEH-P complex.
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