A retrospective study of prognostic markers in bitches diagnosed with pyometra

Kalėms, kurioms diagnozuota piometra, retrospektyvi klinikinių atvejų analizė

MASTER THESIS
of Integrated Studies of Veterinary Medicine

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KAUNAS 2018
THE WORK WAS DONE IN THE DEPARTMENT OF SMALL ANIMAL CLINIC

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# TABLE OF CONTENT

SUMMARY ........................................................................................................................................ 5
SANTRAUKA...................................................................................................................................... 6
ABBREVIATIONS ............................................................................................................................ 7
INTRODUCTION ............................................................................................................................... 8
LITERATURE REVIEW ..................................................................................................................... 9
   Aetiology and pathogenesis ........................................................................................................... 9
   Diagnostic methods of pyometra .................................................................................................. 10
      Clinical signs ................................................................................................................................. 10
      Haematology and biochemical findings ....................................................................................... 10
      Imaging .......................................................................................................................................... 11
   Treatment method .......................................................................................................................... 12
      Surgical treatment methods ......................................................................................................... 12
      Uterine drainage and lavage ........................................................................................................... 12
      Medical treatment ....................................................................................................................... 13
MATERIAL AND METHODS ........................................................................................................... 16
   Investigated parameters ............................................................................................................... 16
   Clinical observations ..................................................................................................................... 16
   Diagnostic tests ............................................................................................................................... 17
      Haematology and biochemical data .............................................................................................. 17
      Imaging .......................................................................................................................................... 18
   Statistical analyses ........................................................................................................................ 18
   Literature review ............................................................................................................................ 18
RESULTS ........................................................................................................................................... 19
   Number, breed, age and type of treatment ..................................................................................... 19
      Breed prevalence .......................................................................................................................... 19
      Age prevalence ............................................................................................................................ 20
      Type of treatment ......................................................................................................................... 21
   Time of clinical signs after oestrus .................................................................................................. 22
   Anamnestic and clinical findings ..................................................................................................... 23
   Haematological and Biochemical findings ....................................................................................... 25
      Prevalence of changes in temperature of bitches with pyometra and relationship with peritonitis .......................................................... 29
      Prevalence of increased CRP in bitches with pyometra ................................................................. 30
      Relationship between C-reactive protein and peritonitis .............................................................. 31
   Mortality and complications .......................................................................................................... 31
DISCUSSION ..................................................................................................................................... 33
A RETROSPECTIVE STUDY OF PROGNOSTIC MARKERS IN BITCHES DIAGNOSED WITH PYOMETRA

Natalie Boström

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SUMMARY

Pyometra is one of the most common disease in intact bitches with a variety of clinical and laboratory findings. If the disease is not detected early, it can be fatal and may lead to complications such as peritonitis or systemic inflammatory response syndrome. The aim of this study was to investigate etiology and manifestation of pyometra and to identify what parameters of clinical signs and blood parameters that are most common in pyometra, what treatment methods that are most common and if there are other options which can be used to keep the bitch intact. Also, to see what diagnostic methods that can be used and which that are most accurate in early diagnosis of pyometra.

A retrospective study was done by using data obtained from Albano animal hospital in Sweden. In the study 119 bitches diagnosed with pyometra during the year 2017 was used. 114 bitches were surgically treated by ovariohysterectomy, 1 were medically treated and 3 were euthanized without treatment. The most common complication observed in bitches treated surgically was peritonitis (n=27).

Vaginal discharges, depression, increased CRP and leucocytosis was most common findings in bitches diagnosed with pyometra. Uterus enlargement was seen in 105 out of 111 bitches and the size varied between 7 to 80 mm. Peritonitis were found in 27 bitches before treatment and in 25 bitches after treatment.

Keywords used: pyometra, surgical treatment, medical treatment, peritonitis.
KALĖMS, KURIOMS DIAGNOZUOTA PIOMETRA, RETROSPEKTYVI KLINIKINIŲ ATVEJŲ ANALIZĖ

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SANTRAUKA

Piometra yra viena iš dažniausiai diagnozuojamų nekastruotų kalių ligų, kuriai būdinga klinikinių ir laboratorinių tyrimų rezultatų įvairovė. Jei liga nėra diagnozuota anksti, ji gali būti mirtina ir gali sukelti komplikacijas, tokias kaip peritonitas ar sisteminis uždegiminis atsako sindromas. Šio tyrimo tikslas buvo ištirti piometros etiologiją ir pasireiškimo ypatumus bei nustatyti, kokie klinikiniai požymiai ir kraujo parametrų pokyčiai yra būdingi sergant piometra, kokie gydymo metodai dažniausiai taikomi ir ar yra kitų galimybių, kurios gali būti naudojamos, kad kalės nesirgtų. Be to, tirti diagnostiniai metodai, kurie gali būti naudojami ir kurie yra tiksliausi ankstyvoje piometros stadijoje.

Duomenys buvo rinkti Albano gyvūnų ligoninėje, Švedijoje. Tyrimui buvo atrinkta 119 kalių, kurioms per 2017 metus buvo diagnozuota piometra. 114 kalių buvo gydytos chirurginiu būdu - atlikta ovariohisterektomija, 1 buvo gydyta skiriant medikamentus ir 3 buvo eutanazuotos be gydymo. Dažniausia komplikacija pasireiškusi kalėms po chirurginio gydymo buvo peritonitas (n = 27).

Išskyros iš maksties, depresija, padidėjęs CRB kiekis ir leukocitozė buvo dažniausiai pokyčiai nustatytu kalėms Sirgusioms piometra. Gimdos padidėjimas buvo nustatytas 105 iš 111 kalių ir dydis svyravo nuo 7 iki 80 mm. Peritonitas buvo diagnozuotas 27 kalėms prieš gydymą ir 25 kalėms po chirurginio gydymo.

Raktažodžiai: piometra, chirurginis gydymas, medikamentinis gydymas, peritonitas.
ABBREVIATIONS

SIRS – systemic inflammatory response syndrome
E.coli – Escherichia coli
CRP – Capillary refill time
SAA – Serum amyloid A
TNFα – Tumour necrosis factor alpha
IL1-IL15 – Interleukin 1-15
MODS – Multiple organ failure
X-ray – Radiographic imaging
OHE – Ovariohysterectomy
PGF\(_2\alpha\) – Prostaglandin F\(_2\) alpha
PR A – Progesterone receptor A
PR B – Progesterone receptor B
TIDA – Tuberoinfundibulum
PAD – Pathological anatomical diagnosis
CRT – Capillary refill time
EDTA – Ethylenediaminetetraacetic acid
ALP – Alkaline phosphatase
ALT - Alanine aminotransferase
Na – Sodium
K – Potassium
Ca – Calcium
Cl – Chloride
GDPR – General data protective regulation
SPSS – Statistical package for the social sciences
CEH – Cystic endometrial hyperplasia
HCT – Hematocrit
Hb – haemoglobin
INTRODUCTION

Pyometra is one of the most common diseases among bitches that are not neutered (3). The disease normally occurs before the age of 10 in 25 per cent of bitches with an average age of 8 years (1,2).

The cause of pyometra is not really known, but some authors have suggested that the cause might be of hormonal influence of estrogen and progesterone on the uterus and ascending bacteria from the bitch normal flora. Most common bacteria found are *Escherichia coli*. Some pathologies of the uterus, such as cystic endometrial hyperplasia (CEH) and mucometra may lead to infection of the uterus and then eventually pyometra (18). Some breeds are more predisposed than others which may indicate that there might be a genetic predisposition in some breeds (3,4).

Different treatment methods can be used to treat pyometra. Most common is ovariohysterectomy, which is used in most cases when a bitch is diagnosed with pyometra (40). Medical treatment is used in some cases and the bitch is then treated with prostaglandins, progesterone receptor antagonists and dopamine agonists, and antibiotics (41).

If the disease is not treated or if diagnosis is done when the disease has progressed to peritonitis or systemic involvement, the prognosis is often worse, and the bitch chance of survival is lowered. Some complications are associated with increased mortality such as systemic inflammatory response syndrome and peritonitis (6). Many dogs are euthanized when diagnosed with pyometra and normally it is due to high age, or if the owner has limited amount of money or if the bitch has other diseases that may increase risk of anesthesia or surgery and decreased chance of recovery. Some studies have reported a mortality rate of 3 to 10 per cent (5). It is important to diagnose the bitch early in the disease to prevent complications and to have a good outcome in the disease. Some biological markers can be investigated to predict pyometra and its outcome.

The aim is to learn more about the clinical signs of pyometra and to study the prevalence in bitches diagnosed in pyometra and try to find what is the cause of pyometra in and peritonitis, and to study what treatment method mostly used and complications of pyometra and treatment.

The goal with this study is:
1. To investigate breed prevalence, what age pyometra occur at and most common treatment methods.
2. To analyse what clinical signs that are most common and when during the oestrus cycle pyometra most commonly is diagnosed.
3. To investigate blood parameters and their relationship with peritonitis and temperature.
4. To investigate what complications that may occur.
LITERATURE REVIEW

Aetiology and pathogenesis

Pyometra is a disease where pus accumulates in the uterus. The disease occurs in intact females and about 25 per cent of bitches get the diagnosis of pyometra before the age of 10, with an average of 8 years (1,2). Pyometra normally occur 4-8 weeks after oestrus, during dioestrus when the uterus is affected by progesterone, produced by corpus lutea. Oestrogen increases the stimulatory effects of progesterone by increasing the number of progesterone receptors and the vascularization in the uterine wall (7). Progesterone starts to stimulate endometrial gland development which leads to increased glandular secretion, it also decreases myometrial contraction which prevents discharges from leaving the uterus via the vagina, this leads to a favourable environment for bacteria (8).

The development of cystic endometrial hyperplasia has been discussed to be one factor that predisposes the uterus to pyometra. But it seems that both CEH and pyometra can occur without the other and that pyometra is mainly caused by a bacterial infection that render the uterus (9). If pyometra is not treated, it may lead to systemic inflammatory syndrome (SIRS) and dysfunction of many organs, that can lead to death if the animal is not treated (4). There might be fluid in the lumen of uterus even without a bacterial infection and then it is called hydrometra, mucometra or hemometra and depends on what type of fluid that can be found in the lumen. Normally there are no clinical signs if no bacterial infection (10).

Gram negative bacteria is the most common bacteria isolated from uterus, these bacteria releases endotoxins when they grow and dies. These endotoxins may be released into the bloodstream and cause systemic inflammatory syndrome (SIRS) and multiple organ dysfunction (MOD). *Escherichia coli* is the most common pathogen isolated from animals with pyometra and it is believed to arise from the normal bacterial flora of the animal (11). The bacteria adhere to the hormonally influenced endometrium in the uterus and leads to the disease (12). Other bacteria that occur in a less extent is, *Klebsiella spp.*, *Citrobacter spp.*, *Proteus spp.*, *Salmonella spp.*, *Pseudomonas spp.*, *Streptococcus spp.*, *Staphylococcus spp.* and *Arcanobacterium pyogenes*. Most of these bacteria are commensals of the bitch normal vaginal flora and reaches the uterus by ascending through cervix from the urogenital tract or spread via other routes of infection such as via the blood (13).

According to some studies, some breeds are more likely to be diagnosed with Pyometra than others, such as Rottweilers, Golden Retriever, Bernese Mountain dog, cavalier king Charles and Collies that suggests that genetic indicators may be involved (3,4).
Diagnostic methods of pyometra

Clinical signs

Pyometra is almost always present during dioestrus and includes a variety of signs that depends on what type of bacteria present in the uterus, if there is an open or closed pyometra and the severity of the disease. The most common clinical signs are polydipsia, polyuria, lethargy, vomiting and/or diarrhea; anorexia, abdominal distension and pain on palpation and vaginal discharges (13). If there is an open pyometra, vaginal discharges are normally seen, and their common features depends on the type of bacteria involved; if mucopurulent or purulent discharges, Streptococcus spp. is usually present; if containing blood, it is often associated with mucoid or haemolytic E.coli (14). Other clinical signs that might be present include: dehydration, hyperthermia or hypothermia; hyperaemic mucus membranes or pale mucus membranes; urinary tract infection or lameness (10).

Systemic inflammatory response

When certain bacteria in the uterus are growing or when they die, they release endotoxins. These endotoxins when entering the bloodstream will cause systemic inflammation which causes a cascade of different immunological reactions in the animal, and this will lead to production of acute phase proteins (C-reactive proteins (CRP), Serum amyloid A (SAA)) by the hepatic cells (15). Pyometra develops into systemic inflammatory response syndrome (SIRS) in almost 6 of 10 cases. (16). To be able to diagnose SIRS, at least 2 or more criteria must be present of the clinical signs; Heart rate >120 bpm, respiratory rate >40 bpm or PaCO₂ <30 mm Hg, temperature <38 °C or >40,1°C, leukocytes concentration in the blood >18000 white blood cells/µL or <5000 white blood cells /µL and band neutrophils percentage.

SIRS can occur with injury or when microbes enter the blood stream (17). CRP and serum amyloid A (SAA), Tumour necrosis factor α (TNF- α), Interleukin 1 (IL-1), interleukin 6 (IL-6), Interleukin7 (IL-7) Interleukin 8 (IL8), Interleukin 10 (IL-10) and Interleukin 15 (IL15) are some biomarkers that have been analysed, to find prognostic markers for SIRS and multiple organ failure (MODS) which often occur in pyometra cases. It is important to recognize SIRS in the patient fast to be able to treat the animal and to have a good outcome and also to prevent the misuse of antibiotics (15,16).

Haematology and biochemical findings

In a study performed in Sweden of 356 bitches diagnosed with pyometra, blood tests showed an elevation of total white blood cells, increased number of neutrophils (increased number of immature neutrophils) or decreased neutrophils, if neutrophils pooled in the uterus which occurs
often in closed pyometra, monocytesis, a mild normochromic, normocytic non-regenerative anaemia (5,18). Leukopenia may be present if the bitch has septicemia or if an uncontrollable infection, and the outcome is considered less positive (7,18). Anaemia of chronic disease occur in inflammatory disorders, such as in chronic infection and is believed to be the cause of toxic effects on the bone marrow and by the increase of erythrocytes in the uterus (13). Thrombocytopenia occur if the animals bone marrow is affected by the toxic events from the infection (7).

An increase in CRP can be seen in animals with infections, neoplasia, immune mediated disorders or tissue injury which causes inflammation. CRP is an acute phase protein and it is not affected by age or gender, steroids, NSAIDs or opioids (19). It is synthesized in the liver by the hepatocytes in response to the ongoing inflammation triggered by cytokines released from macrophages (20). Closed-cervix pyometra has shown to give a higher increase in CRP than open pyometra (21).

Biochemical abnormalities that may occur are: hyperproteinaemia, hyperglobulinemia (due to the inflammation and hypoalbuninemia that are a part of the acute phase reaction); increased ALP, bilirubin and cholesterol occur due to intrahepatic cholestasis and not due to hepatic damage, which would be the result if increased ALT; decreased glucose may indicate SIRS; azotemia due to chronic inflammation that leads to pooling of red blood cells in uterus, supressed production of erythrocytes. Decreased sodium and increased potassium can be seen if the animal vomits or has diarrhea (7,18).

When doing a urinalysis, proteins and urine specific gravity may be increased and bacteria may be found (7). Cytology taken with swabs from the vagina can be done, but should not be the primary diagnosis of pyometra, it is a tool used to identify the bacteria invading the uterus to decide appropriate antibiotics to be used (22).

**Imaging**

**Radiographic imaging**

Radiographic-imaging is used to diagnose pyometra in the bitch but can sometimes mislead us the information needed. If the uterus is enlarged and fluid-filled it is normally seen on radiographs, but if not, it is harder to use this method for this cause, and ultrasound is more accurate. Closed-pyometra leads to a more enlarged uterus than an open-pyometra, this increases the chance of diagnosis with radiographs. On the X-ray picture, a large tubular structure can be seen in the caudo-ventral abdomen, pushing the intestines more cranio-dorsally in abdomen. The animal should be placed in lateral recumbency for the best visibility of the uterus on the X-ray picture (23,7,10).
**Ultrasound**

The most common way to detect pyometra is by doing an ultrasound. With an ultrasound, it is possible to determine thickness of uterine wall, the size and if fluid is present in the uterus even if the diameter of uterus is normal. It is hard to differentiate pyometra from mucometra, hydrometra, and hemometra with an ultrasound, but sometimes the fluid can be said to be serous or viscid (10,8). In the case where clinical signs are not present but there is anechoic luminal content in the uterus, mucometra and hydrometra can be suspected. In pyometra, the luminal contents normally are homogenous or echo-dense and move in a swirling pattern (23). The enlarged uterus can be found in the caudo-ventral abdomen, pushing the intestines more cranial-dorsally (7).

**Treatment method**

**Surgical treatment methods**

The best treatment of a confirmed pyometra is ovariohysterectomy (OHE) for bitches that are not being used for breeding, is affected systemically or if cervix is closed. Ovariohysterectomy removes the source of infection and prevents of pyometra to come back. Sometimes the bitch general condition is needed to be stabilized before the surgery, this is done by administrating intravenous fluids that adjusts the electrolyte and acid-base balance, and a broad-spectrum antibiotic against the most common pathogen in pyometra, if the animal is systemically affected the antibiotic therapy is continued after surgery (24,25). If the animal has azotaemia that cannot be resolved before surgery, the prognosis for the bitch less positive (8). The surgical techniques of pyometra in the bitch is well described in the literature. Surgical treatment of pyometra have been proven to lead to fast recovery of the bitch and normalisation of haematological and biochemical abnormalities.

**Uterine drainage and lavage**

Some studies have been made to try to keep the fertility at the bitch by trying to make the treatment duration shorter and to improve the time of recovery. The procedure is done by making a flushing medium made of a 50:50 mixture of povidoneiodine 100 mg/ml and normal saline, which made a 5 per cent betadine-saline mixture. The bitch is injected with atropine sulphate 0.5 per cent and acetylpromazine maleate 2 per cent. The uterus is entered via a linea alba incision and the uterus is taken out from abdomen. A protoscope was put in the vagina cranially and then the introducer was removed from the protoscope. An insemination pipette with syringe attachment, used for artificial insemination in bovines is introduced via the protoscope and moved cranially through the cervix into the uterus and then adding the medium of 5 per cent betadine-saline mixture.
and flush the uterus, the amount of the medium depends on the size of uterus. The uterus and uterus horns may have to be massaged gently to be able to make the pus in uterus more liquid to be able to be aspirated via the syringe. The procedure is repeated until both horns are flushed and until the aspirated liquid looks more like the medium itself. Uterus is emptied from liquid by massaging the uterus and uterus horns caudally and then pipette is removed from cervix. Vagina is flushed with the medium as well to remove possible pus that collected during the aspiration and emptying of the vagina. Abdominal wall is closed by using same method used for ovariohysterectomy. Antibiotics should be used based on sensitivity testing (26).

**Medical treatment**

Medical treatment with prostaglandins (PGF$_{2\alpha}$), progesterone receptor antagonist (aglepristone) and dopamine agonists (cabergoline, bromocriptine) are used to treat bitches with pyometra without using an invasive procedure (7). Progesterone stops the contractions of the myometrium of uterus and causes cervix to close, which prevents the evacuation of pus from the uterus (27). When pyometra develops in the female, it is often a serious situation that needs to be solved as soon as possible and therefore medical treatment of pyometra is often contraindicated and ovariohysterectomy most commonly recommended. When surgery is not an alternative, medical treatment is an option. Surgical treatment is contraindicated if the bitch is old or if surgery and anesthesia might lead to complications or death (36,5).

Pyometra can be open-cervix or closed-cervix pyometra. Open pyometra with vaginal discharge can be treated medically and closed pyometra is recommended to be treated by surgery, because if treated medically it might rupture and pus can leak out in abdomen and cause peritonitis. It takes 48 hours for some of the used drugs to be effective and during this time, the risk of a ruptured pyometra increases (27). A severely ill patient with peritonitis, sepsis, or a patient that has liver, kidney or cardiac disease, hypothermia/hyperthermia is also not good candidate for medical treatment (27,36,5). Medical treatment is often the choice when the bitch is younger than 5 years of age, clinically healthy, metabolically stable, if cervix is open and no ovarian cysts (22,36).

**Prostaglandins**

The use of low dose prostaglandin elicits relaxation of the cervix and induce contraction of the myometrium immediately, which then allows emptying of the uterus via the vagina. Repeated doses are necessary to fulfil the desired effect to cause luteal regression which normally occur after 5 days and uterine emptying which may occur after 7-14 days. Prostaglandins has luteolytic and uterotonic effect and is the most commonly used drug to treat pyometra in bitches. There are natural
prostaglandins (Dinoprost tromethamine) and synthetic prostaglandins (Cloprostenol sodium) that can be used for treatment of pyometra in bitches. The natural prostaglandin is more effective than synthetic prostaglandins but also has more side effects. If natural prostaglandins are to be used for treatment of the bitch, lower doses should be started with and it can later be increased with each injection. Prostaglandins should not be used in animals with closed cervix pyometra due to the risk of uterine leakage of pus into the abdominal cavity also if the bitch has sepsis, peritonitis, if kidney or liver disease or if the bitch is pregnant. If the bitch gets sicker and the vaginal discharges do not improve, ovariohysterectomy should be performed (28,7,34,29,37, 27).

**Side effects of prostaglandins**

Reactions that may occur with the use of natural or synthetic prostaglandins normally starts within 5 min and lasts up to 1 to 1,5 hour depending on the dose given subcutaneously. Dinoprost tromethamine, which is a natural prostaglandin cause side effects such as salivation, restlessness, vomiting, diarrhea, urination, panting. Synthetic prostaglandins do not cause such severe side effects as natural prostaglandins, but these side effects can be hypersalivation, vomiting and diarrhea. These reactions are caused due to the action of prostaglandin on the smooth muscles. Side effects can be prevented by not feeding the bitch before the injection of prostaglandins and walking the bitch for 15 min after administration (38,28,29,30,18,5).

**Progesterone receptor antagonists**

Progesterone antagonists binds to progesterone receptors (PR-A and PR-B) found in the endometrium and myometrium which prevents binding of progesterone to the uterus and it also removes progesterone that has already bound to the receptors. The concentration of plasma progesterone remains the same, only their effects are blocked. These events lead to supressed biological action of progesterone and causes cervix to open and start parturition in a pregnant bitch. These effects are necessary to treat pyometra with the use of medical management. There are some different drugs used to elicit the anti-progesterone effect: mifepristone, onapristone and aglepristone. Aglepristone is the one approved for veterinary use in most countries to induce of abortion and Mifepristone is only approved in few countries. The effect of antiprogestins are to elicit contractions of uterus and cervical opening, for emptying of uterus, these effects started within 4-48 h in a study done by Fieni (2006) in bitches with closed-cervix pyometra. Aglepristone is also used to induce abortion and to treat vaginal fibroma in the bitch. (Mechanism of action and clinical effects of antiprogestins on the nonpregnant uterus) (32,33, 34).
**Side effects of progesterone receptor antagonists**

Side effects are not common in bitches treated with Aglepristone, some studies show vomiting, but is mostly due to the combination with the severity of the disease. Aglepristone should not be used in animals that have renal or hepatic dysfunction, the bitch should be in a good condition if medical treatment should be applicable to prevent the risk of side effects. If the bitch even thou having hepatic disease, kidney disease or peritonitis, she should be controlled during the whole treatment. Systemic disease seen in the bitch during medical treatment with Aglepristone may lead to severe side effects such as hypothermia, which can be seen in the bitch before parturition when the plasma progesterone concentration is elevated, speak for that Aglepristone has effect on the hypothalamus, restlessness, vomiting, diarrhea, anorexia, depression and local inflammatory reaction after injection (27, 33).

**Dopamine agonists (cabergoline, bromocriptine)**

Dopamine agonists act on the D2-dopamine receptors of lactotrophs in the pituitary gland to inhibit prolactin. Pituitary prolactin secretion is regulated by endocrine neurons in the hypothalamus. The most important of these are the neurosecretory tuberoinfundibulum (TIDA) neurons of the arcuate nucleus that secrete dopamine (aka Prolactin Inhibitory Hormone) to act on the D2 receptors of lactotrophs, causing inhibition of prolactin secretion. Thyrotropin-releasing hormone has a stimulatory effect on prolactin release, however prolactin is the only adenohypophyseal hormone whose principal control is inhibitory (42,43).
MATERIAL AND METHODS

A retrospective study was done based on patient journals from the journal system “Trofast” at Anicura Albano Veterinary hospital in Sweden. Bitches diagnosed with pyometra receives a diagnose code KA4121 used to search after cases with pyometra from the year 2017. A number of 274 journals was received and a total number of 200 bitches was used in the study. The journals were studied, and the data was transferred to an excel table for later analysis. When going through the journals, a number of cases were decided to not to be used in the study: cases from another clinic, when the animal only came to the clinic for surgery of pyometra, or if blood samples were not taken due to young bitch and no severe clinical signs, cost restrictive from the owner, and if the clinical signs were not described, if the animal was diagnosed with mucometra verified on pathological anatomical diagnosis (PAD) or if uterus was not filled with liquid/pus at surgery. This led to a study of 119 cases of pyometra.

Ethical permission was not necessary since this study used journals that already existed in the journal system.

Investigated parameters

Anamnesis was taken at Albano animal hospital by veterinarians and the nurses. Anamnestic data that was used for analyses included breed, age, vaginal discharges, anorexia, depression, polyuria, polydipsia, vomiting, diarrhea, increased/decreased weight and lameness, size of uterus, complications, type of treatment (surgery, medical, euthanasia). Most of the anamnesis was based on the owner’s experience of the dog at home.

Clinical observations

A physical examination was done in each animal to receive as much information about the animal and its clinical status as possible. The anamnestic data that was noted was general condition, mucus membranes, capillary refill time (CRT), temperature, hydration status, abdominal pain, tension, palpable uterus; vaginal discharges and lameness. Also, the size of uterus based on ultrasound and the surgeon’s description was described. Data was only used from the first observations when arriving to the clinic. In the case if the animal was sent home and the came back a few days later, the clinical signs observed when coming back to the clinic was included in the data.

The diagnose peritonitis and ascites was done during ultrasound or during surgery. If during surgery, rupture of uterus was observed or leakage of pus from ovaries, and if the diagnose code
for peritonitis was not mentioned in the patient journal, it was still counted in this analysis as peritonitis.

**Diagnostic tests**

**Haematology and biochemical data**

The data received for haematology and biochemistry was done by withdrawing blood from the animal and then the blood was analysed at the clinic’s own laboratory. The nurses take a blood sample from the cephalic vein in the front leg of the dog. In some cases, the blood might have been taken from the saphenous vein if not able to withdraw blood from front legs. Jugular vein may also have been used, if there was hard to take blood from the legs (i.e. if the animal had bad blood pressure in the veins or if the animal was dehydrated). Sterile material is always used when withdrawing blood. When the animal comes to the clinic and is suspected to have pyometra based on clinical signs, a venous catheter is normally used to withdraw blood and left for further treatment. The site of sample collection is shaved, cleaned and disinfected before putting the venous catheter and collecting the blood. The tubes normally used are serum (biochemistry) and EDTA (haematology) tubes, or if laboratory personal is not present in the clinic or if the veterinarian required a quick analysis, heparin is used instead of serum. EDTA do not need to be centrifuged before testing but should be put on a machine that turns the tube all the time to mix it properly with the EDTA. Serum needs to be centrifuged but should only be done so after 30 minutes. Heparin can be centrifuged after collection and then the plasma is withdrawn into a small container that is used in the machine analysing the biochemical parameters. The data analysed from blood sample was the C-reactive protein (CRP), erythrocytes, haematocrit, haemoglobin, white blood cells, platelets, alkaline phosphatase (ALP), Alanine aminotransferase (ALT), urea, creatinine, albumin, phosphate, sodium (Na), Potassium (K), Calcium (Ca), Chloride (Cl), bile acids, glucose and lactate. Blood tests taken before surgery or medical treatment was chooses for the data analysis used for this thesis. If data were added after the first testing of the blood and before surgery, this data were also analysed.

The blood tests were analysed at the laboratory at Albano animal hospital where the patient journals were obtained. For haematological analyses, Sysmex XN-1000 haematology analyser were used and for biochemical analyses, Hitachi-Roche-Cobas c 311 analyser were used. For the biochemical analyses that was done when the laboratory personal were not present, the haematology was analysed in IDEXX procyte dx™ and the biochemical analyses was done on IDEXX catalyst dx™. Lactate was either tested by the nurse using the “The edge lactate analyser” or by laboratory personal using the Gem premier 3500.
Several analysis equipment was used during the analysis of blood and most of the values were in the same reference value in both machines. If the reference value were not the same, blood tested in each machine is evaluated and mentioned in two different analyses. The number of tests for each machine is mentioned in the table nr 3 and 4.

When the machines have finished the analysing of the blood, the blood values is inserted into the patient journal in the clinics journal system “Trofast”. These data are saved until the clinic decides to delete these data, the owner information is only saved for up to 5 years after the last visit at the clinic due to the general data protective regulation (GDPR) law.

Imaging

Ultrasound

An ultrasound machine was used to perform abdominal ultrasound in bitches coming to the clinic and if the veterinarian suspected pyometra. Pictures were taken of the uterus and saved in the clinics imaging system. The number of bitches analysed with ultrasound were 119. The size of uterus was estimated during the ultrasound or during surgery.

Statistical analyses

The statistical analysis was performed in Excel and Statistical Package for the Social Sciences (SPSS). The limit for statistical significance was set at $p = < 0,05$ to evaluate the significance between groups in different age, what clinical signs and blood parameters that occurred with peritonitis and increased CRP and temperature. Data was collected and analysed by the statistical systems and calculated for average, median, min, max values, percentage and number of animals tested included for each parameter. Diagrams and tables were created in excel or in the SPSS program.

Literature review

Databases as GoogleSchoolar, PubMed, National centre of Biotechnology information was used to find articles relevant in the area of Pyometra. Search words as pyometra, open/closed pyometra, CEH (cystic endometrial hyperplasia), mucometra, bitch, dog, canine, surgical treatment, medical treatment, diagnosis, CRP, peritonitis, sepsis, SIRS, Aglepristone, antiprogestins, progesterone receptor blocker, bromotocropine, cloprostenol, prostaglandin F$_{2a}$, Dopaminergic drugs, treatment and treatment methods were used. Books in veterinary medicine subject was used.
RESULTS

Number, breed, age and type of treatment

Breed prevalence

The total number of bitches included in this study were 119. When analysing the frequency of breed distribution among bitches diagnosed with pyometra in the study group it was noticed that a wide range of different breeds were represented (n=54). Different size of Poodle and Dachshund was estimated as the same breed. Different size of Schnauzer was treated as a separate breed. The most common breed with the highest percentage was Labrador Retriever with 9.2 per cent, the breed with the second highest was Mixed breed with 8.4 per cent, followed by Miniature schnauzer 6.7 per cent, Poodle and Golden Retriever received 5.9 per cent each, French bulldog, Staffordshire bullterrier, Chihuahua received 4.3 per cent and Dachshund, English springer spaniel and French bulldog received 3.4 per cent. Other dogs of different breeds received a lower percentage than two and was counted as others in the diagram. Some of these breeds included (Rottweiler, English pointer, Old English sheepdog, Field spaniel, English bulldog, Kromfohrländer, Samoyed, German spaniel, Havanese, Dalmatian, Japanese spitz, Small Brabant G., Cane corse, German short haired pointing dog, Polish low land dog, Eurasian, Swedish Elk hound, Irish soft coated wheat terrier etc.) had a percentage that ranged between 0.5 and 2. **Figure 1** below shows most common breeds in this group that developed pyometra.

![Prevalence of different breeds diagnosed with pyometra](image)

**Fig. 1.** Demonstrating the most common breeds diagnosed with pyometra.
Age prevalence

Figure 2 shows the most common age groups in bitches diagnosed with pyometra. Out of 119 bitches 5.9 per cent was included in the age group between 1-3 years old, 16.0 per cent was included in the age group between 4-6 years old, 38.7 per cent was included in the age group between 7-9 years, 31.1 per cent was included in the age group of 10-12 years and 8.4 per cent was included in the age group between 13-16 years. The average age of bitches diagnosed with pyometra was 8.5 years. The youngest bitch was 1 year old, and the oldest was 16 years. Seen in figure 2.

Fig.2. Demonstrating the most common age groups of bitches diagnosed with pyometra.
Type of treatment

Out of the 119 bitches diagnosed with pyometra, 1 (0.8 per cent) bitch was medically treated on the owners request, 114 (95.7 per cent) bitches were surgical treated at the hospital the same day or the day after, 3 (2.5 per cent) bitches were euthanized before surgery without treatment due to severe disease, age and on the owners request, 1 (0.8 per cent) bitch were sent to another hospital for surgical treatment. The 6 (5.2 per cent) bitches that were euthanized after surgery, were euthanized due to complications (peritonitis, anaemia) and serious illness not improving after surgery. Seen in figure 3.

Fig. 3. The diagram shows the type of treatment chosen for the bitch after clinical examination and how many that were euthanised after treatment.
Time of clinical signs after oestrus

Clinical signs of pyometra was normally noticed by the owner that brought the dog to the clinic. Sometimes the owner noticed some symptoms of pyometra a few days earlier and in some cases even weeks earlier. The signs the owner normally noticed at home were polyuria/polydipsia, anorexia, vaginal discharges, diarrhea, vomiting and depression. These signs normally occurred during oestrus in 18.8 per cent, in <3 days after oestrus in 11.5 per cent, and in 1-8 weeks after oestrus in 61 per cent, in 9-12 weeks after oestrus in 8.7 per cent of bitches. This information was received from 69 bitches. All cases of pyometra in this study was not included, for the reasons that the owner didn’t know when the bitch was in oestrus, she was breed recently (within 2-6 weeks), pseudo pregnant or in oestrus more than 6 months ago. Seen in figure 4.

![Figure 4](image_url)

**Fig.4.** Time when clinical signs appeared from last oestrus to day of diagnosis
Anamnestic and clinical findings

Table 1. Prevalence of anamnestic and clinical findings in 119 dogs with pyometra. Data was not available for all parameters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of bitches with abnormal findings/total number of bitches with available data</th>
<th>Number of bitches %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anamnesis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal discharges</td>
<td>88/112</td>
<td>78.6 %</td>
</tr>
<tr>
<td>Anorexia</td>
<td>78/102</td>
<td>76.5 %</td>
</tr>
<tr>
<td>Depression</td>
<td>100/112</td>
<td>89.3 %</td>
</tr>
<tr>
<td>Polyuria</td>
<td>38/63</td>
<td>60.3 %</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>66/91</td>
<td>72.5 %</td>
</tr>
<tr>
<td>Vomiting</td>
<td>39/116</td>
<td>33.6 %</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22/116</td>
<td>19.0 %</td>
</tr>
<tr>
<td>Lameness/stiff</td>
<td>8/119</td>
<td>6.7 %</td>
</tr>
<tr>
<td><strong>Clinical signs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased</td>
<td>35/101</td>
<td>34.7 %</td>
</tr>
<tr>
<td>Decreased</td>
<td>6/101</td>
<td>5.9 %</td>
</tr>
<tr>
<td>Normal</td>
<td>60/101</td>
<td>59.4%</td>
</tr>
<tr>
<td>CRT</td>
<td>2/108</td>
<td>1.9 %</td>
</tr>
<tr>
<td>Mucus membranes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pale</td>
<td>13/119</td>
<td>10.9 %</td>
</tr>
<tr>
<td>Hyperaemic</td>
<td>25/119</td>
<td>21.0 %</td>
</tr>
<tr>
<td>Icteric</td>
<td>1/119</td>
<td>0.8 %</td>
</tr>
<tr>
<td>Abdominal pain/tension/structure</td>
<td>74/119</td>
<td>62.2 %</td>
</tr>
<tr>
<td>Enlarged uterus US</td>
<td>105/112</td>
<td>93.8 %</td>
</tr>
<tr>
<td>General condition</td>
<td>97/119</td>
<td>81.5 %</td>
</tr>
<tr>
<td>Mild, moderate, severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td>17/119</td>
<td>14.4 %</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>27/119</td>
<td>22.7 %</td>
</tr>
<tr>
<td>Closed Pyometra</td>
<td>23/111</td>
<td>20.7 %</td>
</tr>
<tr>
<td>Open Pyometra</td>
<td>88/111</td>
<td>79.3 %</td>
</tr>
</tbody>
</table>

CRT= Capillary refill time
Anamnestic data was obtained by the veterinarian asking the owner questions, some was obtained by the veterinarian. Clinical signs were obtained by the veterinarian while doing a clinical examination of the animal.

The most common clinical signs present in bitches with pyometra was collected from the patient journals and analysed by using SPSS and excel. In Table 1 “Prevalence of anamnestic and clinical findings” the data includes the number of bitches with abnormal clinical findings and total number of animals included for the analysis and the percentage. As shown, for the anamnestic parameters, vaginal discharges can be seen in 78.6 per cent, anorexia 76.5 per cent, depression 89.3 per cent, polyuria 60.3 per cent, polydipsia 72.5 per cent, vomiting 33.6 per cent and diarrhea in 19.0 per cent. 6.7 per cent of the dogs showed lameness. In the parameters for physical examination Increased temperature was present in 34.7, decreased in 5.9 per cent and normal in 59.4 per cent. Pale mucus membranes were present in 10.9 per cent bitches, hyperaemic in 21.0 per cent and 0.8 per cent of bitches had icteric mucus membranes. When palpating the abdomen, many dogs reacted by tension of abdomen and showing discomfort that was interpreted as pain in the journal. Also, during palpation, in many cases, the veterinarian could feel a structure within the abdomen. Abdominal tension, pain and abdominal structure were calculated within the same group since these variables occurred together in most cases and it showed an occurrence of 82.2 per cent. The animal’s general condition was evaluated as mild, moderate and severe and showed that the general condition was mildly changed in 52.1 per cent, moderate changed in 26.1 per cent and severely changed in the bitch in 3.4 per cent. Ascites were present in 14.3 per cent of bitches and peritonitis occurred in 22.7 bitches before treatment. Uterus was enlarged in 93.8 per cent of bitches, evaluated during ultrasound before treatment or during surgery. Closed pyometra occurred in 20.7 per cent of bitches and open pyometra occurred in 79.3 per cent.
Haematological and Biochemical findings

The presence of haematological and biochemical clinical findings is shown in table 2.

*Table 2. Haematological and biochemical clinical findings in 119 bitches with pyometra. Haematology was analysed with Sysmex XN-1000 Haematology Analyser and IDEXX procyte dx™ and biochemistry was analysed with Hitachi-Roche-Cobas c 311 and IDEXX catalyst dx™ analyser.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of bitches with abnormal findings / total number of bitches with available data</th>
<th>Number of bitches with respective findings %</th>
<th>Normal references for Sysmex XN-1000 and Cobas c 311</th>
<th>Normal references for IDEXX procyte dx™ and IDEXX catalyst dx™</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>67/76</td>
<td>88.2 %</td>
<td>&lt;20</td>
<td>5,7-8,9</td>
<td>mg/L</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>36/115</td>
<td>31.3 %</td>
<td>5,7-8,9</td>
<td>5,7-8,9</td>
<td>x10¹²/L</td>
</tr>
<tr>
<td>Hct</td>
<td>44/115</td>
<td>38.2 %</td>
<td>37-62</td>
<td>37-62</td>
<td>%</td>
</tr>
<tr>
<td>Hb</td>
<td>39/115</td>
<td>33.9 %</td>
<td>131-205</td>
<td>131-205</td>
<td>g/L</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>76/115</td>
<td>66.1 %</td>
<td>5-16,8</td>
<td>5-16,8</td>
<td>x10⁹/L</td>
</tr>
<tr>
<td>Thrombocytes</td>
<td>36/115</td>
<td>31.3 %</td>
<td>148-484</td>
<td>148-484</td>
<td>x10⁹/L</td>
</tr>
<tr>
<td><strong>Biochemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>16/115</td>
<td>13.9 %</td>
<td>3,7-6,6</td>
<td>4,1-7,9</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>27/108</td>
<td>25.0 %</td>
<td>3,0-9,0</td>
<td>2,5-9,6</td>
<td>mmol/L</td>
</tr>
<tr>
<td>ALP</td>
<td>49/108</td>
<td>45.3 %</td>
<td>&lt;1,4</td>
<td>23-212</td>
<td>IU/L</td>
</tr>
<tr>
<td>ALT</td>
<td>20/115</td>
<td>17.4 %</td>
<td>&lt;1,2</td>
<td>10-100</td>
<td>IU/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>3/114</td>
<td>2.6 %</td>
<td>&lt;135</td>
<td>44-159</td>
<td>μmol/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>34/108</td>
<td>31.4 %</td>
<td>30-45</td>
<td>23-40</td>
<td>g/L</td>
</tr>
<tr>
<td>Phosphate</td>
<td>4/59</td>
<td>6.8 %</td>
<td>0,7-1,9</td>
<td></td>
<td>mg/dL</td>
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<tr>
<td>Total Protein</td>
<td>33/114</td>
<td>28.9 %</td>
<td>49-71</td>
<td>52-82</td>
<td>g/L</td>
</tr>
<tr>
<td>Bile acids</td>
<td>7/62</td>
<td>11.3 %</td>
<td>&lt;20</td>
<td></td>
<td>μmol/L</td>
</tr>
<tr>
<td>Na</td>
<td>6/108</td>
<td>5.5 %</td>
<td>138-149</td>
<td>144-160</td>
<td>mmol/L</td>
</tr>
<tr>
<td>K</td>
<td>5/107</td>
<td>4.6 %</td>
<td>3,4-4,8</td>
<td>3,5-5,8</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Ca</td>
<td>5/62</td>
<td>8.0 %</td>
<td>2,4-3</td>
<td></td>
<td>mmol/L</td>
</tr>
<tr>
<td>Cl</td>
<td>2/46</td>
<td>4.3 %</td>
<td></td>
<td>109-122</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Lactate</td>
<td>1/5</td>
<td>20 %</td>
<td>&lt;2</td>
<td></td>
<td>mmol/L</td>
</tr>
</tbody>
</table>

*CRP= C-reactive protein, Hct= haematocrit, Hb= Haemoglobin, ALP=Alkaline phosphate, ALT=Alanine aminotransferase, Na=Sodium, K=Potassium, Ca=Calcium, Cl=Chloride*
Table 2 shows the haematological and biochemical clinical findings with the number of abnormal findings and the total number of dogs analysed. Haematology (Erythrocytes, haematocrit, haemoglobin, leukocytes, thrombocytes) were analysed with Sysmex XN-1000 Haematology Analyser and IDEXX procyte dx™ and biochemical values (Glucose, urea, alkaline phosphate, alanine aminotransferase, creatinine, phosphate, total proteins, bile acids, sodium, potassium, calcium and chlorine) were analysed with Hitachi-Roche-Cobas c 311 and IDEXX catalyst dx™ analyser. CRP was increased with 88.2 per cent of the controlled bitches, erythrocytes was abnormal in 36 animals (increased in 4 bitches and decreased in 32), haematocrit was abnormal in 44 bitches (2 increased and 42 decreased), 39 bitches had abnormal haemoglobin (3 had increased, 36 decreased), leukocytes were increased in 64.3 per cent and decreased in 1.2 per cent of bitches, urea was increased in 11 (10.2 per cent) bitches and decreased in 16 (14.8) bitches, thrombocytes was decreased in 17 (14.8 per cent) bitches and decreased in 19 (16.5 per cent), alkaline phosphate were increased in 48 (44.4 per cent) and decreased in 1 (0.9 per cent), alanine aminotransferase was increased in 18 (15.7 per cent) and decreased in 2 (1.7 per cent), total protein was increased in 33 (28.9) bitches, albumin was decreased in 31 (28.7 per cent) of bitches and increased in 3 (2.8), 7 (1.8 per cent) had increased bile acids. Sodium, potassium, calcium and chloride were increased between 4 to 8 per cent. Lactate were only tested in 5 bitches and 1 bitch had increased lactate and was euthanized after surgery. 3 bitches were tested for lactate after surgery and 1 bitch showed an increase in lactate, they were not tested before surgery and not included in the study.
Table 3. Haematology and Clinical biochemistry findings in 76 bitches with pyometra. average, median, normal reference range. Haematology parameters were analysed with “Sysmex XN-1000 Haematology Analyser” and biochemical parameters were analysed with “Hitachi-Roche-Cobas c 311 analyser”. Lactate was analysed with “The edge lactate analyser” or “Gem premier 3500”.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of tests</th>
<th>Average</th>
<th>Median</th>
<th>Min-Max</th>
<th>Unit</th>
<th>Normal reference range</th>
</tr>
</thead>
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<td><strong>Haematology</strong></td>
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<td></td>
<td></td>
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<tr>
<td>CRP</td>
<td>68</td>
<td>146</td>
<td>143</td>
<td>3-350</td>
<td>mg/L</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>72</td>
<td>6,2</td>
<td>6,2</td>
<td>3,9-10,1</td>
<td>x10^{12}/L</td>
<td>5,7-8,9</td>
</tr>
<tr>
<td>Hct</td>
<td>72</td>
<td>37,6</td>
<td>38</td>
<td>4,1-63</td>
<td>%</td>
<td>37-62</td>
</tr>
<tr>
<td>Hb</td>
<td>72</td>
<td>138,5</td>
<td>142,5</td>
<td>22,3-230</td>
<td>g/L</td>
<td>131-205</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>72</td>
<td>21,1</td>
<td>18,1</td>
<td>1,3-75,6</td>
<td>x10^9/L</td>
<td>5-16,8</td>
</tr>
<tr>
<td>Thrombocytes</td>
<td>72</td>
<td>299,3</td>
<td>270,5</td>
<td>15-859</td>
<td>x10^9/L</td>
<td>148-484</td>
</tr>
<tr>
<td><strong>Biochemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>72</td>
<td>5,5</td>
<td>5,5</td>
<td>2,7-8,1</td>
<td>mmol/L</td>
<td>3,7-6,6</td>
</tr>
<tr>
<td>Urea</td>
<td>67</td>
<td>5,3</td>
<td>4</td>
<td>2,0-19,0</td>
<td>mmol/L</td>
<td>3,0-9,0</td>
</tr>
<tr>
<td>ALP</td>
<td>67</td>
<td>15,9</td>
<td>2,1</td>
<td>0,3-278</td>
<td>IU/L</td>
<td>&lt;1,4</td>
</tr>
<tr>
<td>ALT</td>
<td>72</td>
<td>14,8</td>
<td>0,55</td>
<td>0,1-466</td>
<td>IU/L</td>
<td>&lt;1,2</td>
</tr>
<tr>
<td>Creatinine</td>
<td>72</td>
<td>72</td>
<td>66</td>
<td>30-270</td>
<td>µmol/L</td>
<td>&lt;135</td>
</tr>
<tr>
<td>Albumin</td>
<td>67</td>
<td>29,8</td>
<td>31</td>
<td>15-42</td>
<td>g/L</td>
<td>30-45</td>
</tr>
<tr>
<td>Phosphate</td>
<td>62</td>
<td>1,2</td>
<td>1,2</td>
<td>0,6-2,2</td>
<td>mg/dL</td>
<td>0,7-1,9</td>
</tr>
<tr>
<td>Proteins</td>
<td>71</td>
<td>68,7</td>
<td>68</td>
<td>45-92</td>
<td>g/L</td>
<td>49-71</td>
</tr>
<tr>
<td>Bile acids</td>
<td>61</td>
<td>8,8</td>
<td>4</td>
<td>0-69</td>
<td>µmol/L</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Na</td>
<td>67</td>
<td>145</td>
<td>146</td>
<td>136-153</td>
<td>mmol/L</td>
<td>138-149</td>
</tr>
<tr>
<td>K</td>
<td>67</td>
<td>4,2</td>
<td>4,1</td>
<td>3,3-5,9</td>
<td>mmol/L</td>
<td>3,4-4,8</td>
</tr>
<tr>
<td>Ca</td>
<td>62</td>
<td>2,6</td>
<td>2,55</td>
<td>2,1-3,6</td>
<td>mmol/L</td>
<td>2,4-3</td>
</tr>
<tr>
<td>Cl</td>
<td>5</td>
<td>114</td>
<td>114</td>
<td>113-116</td>
<td>mmol/L</td>
<td>109-122</td>
</tr>
<tr>
<td>Lactate</td>
<td>5</td>
<td>1,7</td>
<td>1,4</td>
<td>1,1-3,5</td>
<td>mmol/L</td>
<td>&lt;2</td>
</tr>
</tbody>
</table>

CRP= C-reactive protein, Hct= haematocrit, Hb= Haemoglobin, ALP=Alkaline phosphate, ALT=Alanine aminotransferase, Na=Sodium, K=Potassium, Ca=Calcium, Cl=Chloride.
Table 4. Haematology and Clinical biochemistry findings in 41 bitches with pyometra. Average, Median, Normal reference range. Haematology were analysed with IDEXX procyte dx™ and biochemical parameters were analysed with IDEXX catalyst dx™. Lactate was analysed with The Edge Lactate Analyser or the Gem premier 3500.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of tests</th>
<th>Average</th>
<th>Median</th>
<th>Min-Max</th>
<th>Unit</th>
<th>Normal reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Haematology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>41</td>
<td>6,4</td>
<td>6,48</td>
<td>3,6-9,31</td>
<td>x10¹²/L</td>
<td>5,7-8,9</td>
</tr>
<tr>
<td>Hct</td>
<td>41</td>
<td>39,5</td>
<td>39,8</td>
<td>3,7-56,3</td>
<td>%</td>
<td>37-62</td>
</tr>
<tr>
<td>Hb</td>
<td>41</td>
<td>14,7</td>
<td>140</td>
<td>79-206</td>
<td>g/L</td>
<td>131-205</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>41</td>
<td>20,5</td>
<td>19,4</td>
<td>7,58-64,95</td>
<td>x10⁹/L</td>
<td>5-16,8</td>
</tr>
<tr>
<td>Thrombocytes</td>
<td>41</td>
<td>301,2</td>
<td>286</td>
<td>79-766</td>
<td>x10⁹/L</td>
<td>148-484</td>
</tr>
<tr>
<td><strong>Biochemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>41</td>
<td>5,8</td>
<td>5,66</td>
<td>3,99-10</td>
<td>mmol/L</td>
<td>4,1-7,9</td>
</tr>
<tr>
<td>Urea</td>
<td>41</td>
<td>4,2</td>
<td>3,5</td>
<td>1,1-12,9</td>
<td>mmol/L</td>
<td>2,5-9,6</td>
</tr>
<tr>
<td>ALP</td>
<td>41</td>
<td>199</td>
<td>136</td>
<td>10-2000</td>
<td>IU/L</td>
<td>23-212</td>
</tr>
<tr>
<td>ALT</td>
<td>39</td>
<td>54,7</td>
<td>41</td>
<td>10-206</td>
<td>IU/L</td>
<td>10-100</td>
</tr>
<tr>
<td>Creatinine</td>
<td>41</td>
<td>83</td>
<td>75</td>
<td>29-187</td>
<td>µmol/L</td>
<td>44-159</td>
</tr>
<tr>
<td>Albumin</td>
<td>41</td>
<td>30,3</td>
<td>29</td>
<td>24-79</td>
<td>g/L</td>
<td>23-40</td>
</tr>
<tr>
<td>Proteins</td>
<td>41</td>
<td>74,6</td>
<td>75</td>
<td>59-93</td>
<td>g/L</td>
<td>52-82</td>
</tr>
<tr>
<td>Bile acids</td>
<td>1</td>
<td>200</td>
<td>200</td>
<td>200-200</td>
<td>µmol/L</td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>41</td>
<td>157,7</td>
<td>151</td>
<td>144-157</td>
<td>mmol/L</td>
<td>144-160</td>
</tr>
<tr>
<td>K</td>
<td>41</td>
<td>4,1</td>
<td>4,2</td>
<td>3,2-5,1</td>
<td>mmol/L</td>
<td>3,5-5,8</td>
</tr>
<tr>
<td>Cl</td>
<td>41</td>
<td>113,3</td>
<td>113</td>
<td>106-119</td>
<td>mmol/L</td>
<td>109-122</td>
</tr>
</tbody>
</table>

CRP= C-reactive protein, Hct= haematocrit, Hb= Haemoglobin, ALP=Alkaline phosphate, ALT=Alanine aminotransferase, Na=Sodium, Ca=Calcium, Cl=Chloride.
Haematology and clinical biochemistry findings from bitches with pyometra are presented in Table 3 and table 4 above. Table 3 covers blood analysis from Sysmer XN-1000 and Hitachi-Roche Cobas c311 and table 4 covers blood analysis from IDEXX procyte dx™ and IDEXX Catalyst dx™. Lactate in table 3 were analysed with The Edge Lactate analyser or Gem premier 3500. Different blood analysis machines were used because the laboratory personal were not present in the evening and the personal then used other machines to analyse the blood tests. In table number 3, a number of 72 bitches were analysed, but not all were tested for all parameters. In table 4, 41 bitches were analysed for all parameters except bile acids and ALT.

Prevalence of changes in temperature of bitches with pyometra and relationship with peritonitis

Of the 119 bitches diagnosed with pyometra, 101 bitches were checked for temperature. 59.4 per cent had normal temperature. 34.7 per cent had increased temperature. 5.9 per cent had decreased temperature. Seen in figure 5 below.

Out of the 27 bitches with peritonitis 7 (26.0 per cent) had increased temperature, 0 bitches had decreased temperature and 12 (44.0 per cent) had normal temperature. 8 (30.0 per cent) animals with peritonitis had unknown temperature, figure 6.

**Fig. 5.** Shows the occurrence of changes in temperature in bitches with pyometra before treatment.
**Fig. 6.** Shows the relationship between peritonitis and temperature

**Prevalence of increased CRP in bitches with pyometra**

**Table 5. Data of C-reactive protein in bitches with pyometra.**

<table>
<thead>
<tr>
<th>CRP</th>
<th>Number of animals/total number of animals</th>
<th>Number of animals per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>9/76</td>
<td>11.8</td>
</tr>
<tr>
<td>Increased</td>
<td>67/76</td>
<td>88.2</td>
</tr>
</tbody>
</table>

Of the 76 bitches where C-reactive protein (CRP) were analysed, 67 (88.2 per cent) had increased CRP and 9 (11.8 per cent) had normal CRP at the time of pyometra.
Relationship between C-reactive protein and peritonitis

Increased CRP was found in 20 bitches with peritonitis and it gave a \textit{p-value} of 0.276 which is not significant. CRP was also increased in 48 bitches with no peritonitis. CRP was unknown in 6 bitches with peritonitis. In 8 of the bitches analysed, CRP was normal, and they had no peritonitis. In 1 bitch with peritonitis, CRP was normal. The relationship can be seen in \textbf{figure 7} below.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{relationship_crp_peritonitis.png}
\caption{The relationship between peritonitis and CRP.}
\end{figure}

\textbf{Mortality and complications}

Among those 114 bitches treated surgically with ovariohysterectomy 1 (0.9 per cent) was euthanized during surgery because of tumours in liver and spleen and the conclusion were that it was a bad prognosis for the dog and the owner was informed about the situation and agreed on euthanasia, 5 (4.4 per cent) was euthanized after surgery because they didn’t get healthy from pyometra/peritonitis and their health status worsened. 3 (2.5 per cent) of the bitches was euthanized without treatment, because of severe disease and marked general status. 16 (13.5 per cent) bitches hade other diseases such as splenic tumour, heart disease, corp al or liver tumour, glaucoma, uveitis, urinary tract infection and was operated.

Complications that occurred after surgery could be peritonitis, abdominal tension and pain, respiratory distress, inappetence, vomiting, diarrhea, anaemia, abdominal drainage of fluid and
blood, hypothermia, bleeding from ligatures, these complications occurred in 28 (25.6 per cent) bitches and diarrhea alone occurred in 28 bitches (24.5 per cent) after surgical treatment.

Antibiotics was used in 27/27 bitches with peritonitis ($p=0.001$).

**Table 6.** Total number, mortality, number of bitches diagnosed with peritonitis before surgery and after surgery or that had prolonged hospitalisation, treated surgically or medically.

<table>
<thead>
<tr>
<th>Variables</th>
<th>$N$</th>
<th>Mortality</th>
<th>Peritonitis before</th>
<th>Peritonitis after</th>
<th>Prolonged hospitalisation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$n$ (%)</td>
<td>surgery $n$ (%)</td>
<td>surgery $n$ (%)</td>
<td></td>
</tr>
<tr>
<td>Total number</td>
<td>119</td>
<td>6</td>
<td>27 (22.7)</td>
<td>25 (21.9)</td>
<td>28</td>
</tr>
<tr>
<td>Medically treated</td>
<td>1</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>Surgically treated</td>
<td>114</td>
<td>6 (5.2)</td>
<td>25 (21.9)</td>
<td>25 (21.9)</td>
<td>28</td>
</tr>
<tr>
<td>Euthanized with no treatment</td>
<td>3</td>
<td>3 (2.5)</td>
<td>2 (1.7)</td>
<td>1 (0.9)</td>
<td>1</td>
</tr>
</tbody>
</table>

Peritonitis occurred in 27 (22.7 per cent) before surgery in the 119 bitches diagnosed with pyometra. 25 (21.9 per cent) bitches had peritonitis after surgery and 1 (0.9 per cent) bitch was euthanized after surgery due to peritonitis. Prolonged hospitalization (>3 days) was observed in 28 bitches after surgery and one bitch was euthanized during the hospitalization.
DISCUSSION

This study is based on 119 bitches diagnosed with pyometra. The study material used is taken from one clinic in Sweden and includes bitches diagnosed with pyometra during the year 2017.

To be able to determine why pyometra develops, it is important to look at all factors possible.

**Bree, Age, Time of clinical signs**

Many studies done before, have evaluated breed occurrence and genetically predisposition among certain breeds in cases with pyometra. One study done by Ragnevi Hagman (2004), showed that Bernese Mountain Dog, Rottweiler, Collie (rough haired), Cavalier King Charles Spaniel, Golden Retriever and English Cocker Spaniel had increased risk of developing pyometra. Breeds with decreased risk were Swedish hound, normal size Dachshund and miniature Dachshund, German Shepherd dog and Drever. A reduced risk for mixed-breed dogs have also been shown by Niskanen and Thrushfield (1998). A study done by Francis. O.Smith (2006) also showed an increased risk for: Golden Retriever, Miniature Schnauzer, Irish terrier, Bernease Mountain Dog and Airdale terrier. In present study, a number of 54 breeds were included and the most common breeds diagnosed with pyometra were: Labrador Retriever, Mixed breeds, Miniature Schnauzer, different size of Poodle, Golden Retriever, French Bulldog, Stafford shire Bull Terrier and chihuahua. These results are similar to those of previous researchers. The result might be affected by the different types of breeds that might be more common in certain regions than others for example in the city where chihuahua probably is more common than on the country side. Mixed breed was the second most common breed in this study, while Niskanen and Thrushfield (1998) found in their study that pyometra was not that common in Mixed breeds.

The most common age group in this study was obtained in bitches between 7-9 years old (38.7 per cent). The average age was 8.5 years and the youngest bitch was 1 year old and the oldest 16 years old. Previous studies showed a similar result to the result in this study. In one study done by Fransson et al. (2004), it was showed that the average age of pyometra was 8.4 years, and Egenvall et al. (2001), wrote that the range of age was between 4 months and 18 years. Why bitches develop pyometra when they get older is not really known. But one theory is that the hormonal stimulation on uterus that is repeated with each cycle is increasing the risk of pyometra with age.

The administration of steroid hormones (progestins and oestrogen) used to induce abortion might increase the risk of pyometra, and this might be one of the causes why young individuals develop pyometra at young age (8).

Clinical signs most commonly were observed 1-8 weeks (61 per cent) after oestrus, and in 18.8 per cent of cases pyometra occurred during oestrus. 69 bitches were included in this study, in many
cases, the owner didn’t know when the female was in oestrus last time and was not included in the data. The signs the owner normally noticed before seeking medical care for the dog were polyuria/polydipsia, anorexia, vaginal discharges, diarrhea, vomiting and depression and sometimes the owner noticed some signs weeks before coming to the clinic, which might lead to misinformation for the received data. Most studies that have been done, show that the most common time of pyometra is during the dioestrus in the bitch reproductive cycle (23).

The increase in progesterone during end of oestrus and beginning of dioestrus (with peak at 15 to 30 days after ovulation), results in endometrial proliferation and uterine glandular secretion, decreased myometrial contraction and induces closure of cervix, this increases the risk of bacterial growth in the uterus which makes it a favourable place for bacterial growth (7,36). Due to repeated stimulation of hormones on the uterus, the risk of developing pyometra increases with age (8, 23). In this study many cases of pyometra occurred during the end of oestrus (in 18.8 per cent of cases) which may indicate bacterial ascendance from the normal flora of vagina or urinary tract during proestrus or oestrus (24).

The most common clinical signs present in >50 per cent of bitches included vaginal discharges, anorexia, depression, polydipsia, and polyuria (Table 1), which reflects systemic involvement, in most bitches and supports previous studies by Jitpean et al. (2014). Vaginal discharges were present in 88 (78.6 per cent) of bitches and was absent in 24 bitches (21.4 per cent). Closed pyometra, when vaginal discharges are absent, normally indicates more severe disease (39).

Laboratory findings

Laboratory findings in this study showed that 88.2 per cent had increased CRP which is supported by studies done by Jitpean (2015), B.A. Fransson (2004) and many others. R.Dabrowski et al. (2013) did a study where it was showed that CRP was more increased in bitches with closed-cervix pyometra. The results obtained in this study is supported by the data from the previous study where closed-pyometra had an average of 181 in CRP and open-pyometra had an average of 143 in CRP. Decreased erythrocytes, haematocrit and haemoglobin was found in this study in 32-36 bitches. Anemia is thought to be the caused by the long duration of the disease, erythrocytes are decreased due to the toxic effects on the bone marrow that occur or lack of iron in the blood or and also due to the loss of erythrocytes to the uterine lumen (18). Dehydration can interfere with the evaluation of anemia, if the animal is dehydrated, a misleading value can be received, and a higher haematocrit is obtained. Increased leukocytes and ALP were also common findings in this study. Increased leukocytes was found in 66.1 per cent and is a common finding in bitches according to R.Hagman (2012) and many other authors. Leucocytosis is an indicative of sepsis and can be found elevated early in the disease. When the disease worsens, the presence of band and toxic neutrophils
can be seen (17). Leukopenia was found in 2 bitches which have been found to be an indicative of poorer prognosis (18), in this study both bitches (Labrador Retriever and Golden Retriever) with leukopenia had hyperaemic mucus membranes, closed-cervix pyometra and one of them also had circulatory shock and ruptured uterus. Increased ALT and proteins were seen in 16 to 29 per cent and albumin was decreased in 28.7 per cent.

**Treatment Methods**

Most animals are treated surgically, and some are treated medically. Many authors discuss treatment methods used for animals that are young and has an open-cervix pyometra and a normal organ function where the owner wants to preserve the bitch reproductive tract. These bitches can be treated medically with prostaglandins, progesterone receptor antagonists and dopamine agonists together with antibiotics. Bitches that received medical treatment and that are not breed and conceive may have a higher chance of getting pyometra again at the next cycle according to *Frances O. Smith* (2006). *F.Fieni* (2006) studied the efficacy of Aglepristone with or without cloprostenol in bitches with pyometra. The author followed up on those that were 23 bitches that were successfully treated after 24 months, 3 bitches developed pyometra after 7 to 12 months and 1 bitch after 19 months. Two bitches out of the 23 that received Aglepristone together with cloprostenol did not show occurrence of pyometra at the next oestrus cycle. After 6 years, 3 bitches still didn’t have reoccurrence of pyometra and had normal oestrus.

Ovariohysterectomy is done in most animals and is recommended if the bitch is older or affected systemically, or if increased risk of anesthesia or surgery due to other diseases. In this study 114 bitches were surgically treated by ovariohysterectomy and 6 bitches were euthanized after surgery due to peritonitis or because their health status did not improve after surgery. In one study done by *Jitpean et al.* (2014) complications was observed in 19 per cent of bitches and prolonged hospitalization (>3 days) in 25 per cent. Peritonitis was observed in 13 per cent of bitches, which is a bit lower than received in this study where peritonitis occurred in 21.9 per cent. Prolonged hospitalization on the other hand was observed in 25 per cent in present study, which supports these of previous study by *Jitepean et al* (2006).
CONCLUSION

1. Labrador retriever (9.2 per cent), mixed breed (8.4 per cent) and Miniature Schnauzer (6.7 per cent) was the most common breed diagnosed with pyometra in this study. Most common age group was 7-9 years (38.7 per cent). The most common treatment method used was ovariohysterectomy (95.7 per cent).

2. Vaginal discharges, anorexia, depression, polyuria, and polydipsia could be seen in more than 50 per cent of bitches diagnosed with pyometra. Pyometra was most commonly diagnosed (in 61 per cent of bitches) 1-8 weeks after oestrus.

3. Increased CRP (88.2 per cent), leucocytosis (64.3 per cent), increased ALP (44.4 per cent), decreased erythrocytes (27.8 per cent), decreased haematocrit (36.5) and decreased haemoglobin (31.3), was the most common parameters found in bitches diagnosed with pyometra. The prevalence of increased temperature in bitches with peritonitis was 26 per cent and 5.9 per cent had decreased temperature. Increased CRP was seen in 20 bitches with peritonitis (p=0.276) which is not significant.

4. The most common complication that occurred after ovariohysterectomy was peritonitis (21.9 per cent) and diarrhea occurred in 24.5 per cent after surgery.
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