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Dr. Manish Kumar
M.V.Sc Scholar, Department of
Veterinary Gynaecology and
Obstetrics, Post Graduate
Institute of Veterinary
Education and Research, Jaipur,
Rajasthan University of
Veterinary and Animal Science,
Bikaner, Rajasthan, India

Dr. Pooja
Assistant Professor, Department
of Veterinary Gynaecology and
Obstetrics, International
Institute of Veterinary
Education and Research, Bahu
Akbarpur, Rohtak, Haryana,
India

Corresponding Author:
Dr. Pooja
Assistant Professor, Department
of Veterinary Gynaecology and
Obstetrics, International
Institute of Veterinary
Education and Research, Bahu
Akbarpur, Rohtak, Haryana,
India

Pyometra in different species of animals: A review

Dr. Manish Kumar and Dr. Pooja

Abstract

Pyometra is an acute or chronic inflammatory condition of endometrium. Pyometra usually occurs following an abnormal parturition, uterine infection and a tardy involution of the uterus. It is also thought that progesterone-mediated cystic endometrial hyperplasia (CEH), which is the pathological expansion and proliferation of endometrial glands, predisposes the animal to pyometra. Symptoms of pyometra includes constant or irregular discharge from vaginal with purulent or mucopurulent exudates. While in some cases cervix remains closed and no any discharge is present. Most of the cases pyometra follows a retained placenta and postpartum metritis, in which case there is frequently an intermittent discharge of pus from the vagina. In pyometra the uterine walls are usually thick and heavy and lack tone. Common treatment followed is administration of PGF_{2α} to stimulate uterine defense mechanisms endometritis Treatment is done with PGF₂ or a synthetic analogue for corpus luteum destruction and progesterone source removal.

Keywords: Pyometra, cystic endometrial hyperplasia, pus discharge, endometritis

Introduction

An acute or chronic inflammatory process of endometrium is identified by a uterus filled with pus, corpus luteum (CL) presence, cervix is closed and estrus expression failure is called pyometra (Sheldon *et al.*, 2006) [32]. In some cases complete occlusion of cervical lumen is not seen and the discharge purulent in nature can be observed in the vagina as animal lies down, urinates or defecate (Praveen Raj *et al.*, 2015) [25]. In the presence of a contaminated uterus Pyometra may be seen as a sub-set of endometritis when cows ovulate (Chapwanya 2008) [8]. A rise in the number of An increased amount of pathogenic bacteria present within the uterus as corpus luteum forms and will results in occurrence of pyometra (Noakes *et al.*, 1990) [23]. Luteal phase Prolongation may be due to luteotrophic prostaglandin (PGE₂) increased concentration which is associated with bacterial infection in endometrium (LeBlanc 2008) [19]. Pyometra mainly occurs in cows, bitches, queens, mares, rabbits, ferrets, rats, hamsters and guinea pigs. Incidence of pyometra is low in ewes and sows. Pyometra is quite common in cows and bitches. It occurs mostly commonly during the early phase of postpartum period (15-50 days postpartum). The amount of pus varies from 1-20 litres leading to distension of uterus and uterine horns in cattle. Equine pyometra is similar to a pseudo pregnancy it has massive economic losses to the breeders (Brincko *et al.*, 2011) [31].

Predisposing factors

Pyometra usually occurs following an abnormal parturition, uterine infection and a tardy involution of the uterus. Some conditions like abortion, birth as a premature, twin birth, dystocia, placenta retention, postpartum metritis or septic metritis occurs more commonly when the semen does not contain antibiotics. In rare instances pyometra may develop secondary to mucometra in a heifer with an imperforate hymen that has been bred by a bull or artificially inseminated and infection is introduced into the genital tract through coitus or infected semen.

Under these conditions entry and replication of large number of bacteria (pathogenic in nature) increases rapidly inside the uterus. In all postpartum animals (90%) the uterus is bacteria contaminated after parturition but it does not necessarily signals any infection or uterine disease development. eliminate of pathogenic bacterial contamination in most of these animals happens during the involution process of uterus but some time contamination is not eliminated due to uterine defence mechanisms error it which results in persistent infection ultimately causing pyometra.

In most cases pyometra is a consequence of endometritis because the active corpus luteum in the postpartum animals with this issue causes them to ovulate and develop pyometra. Therefore, the animals may be predisposed to these conditions by the early postpartum ovulation. Gram-negative, anaerobic, and pyrogenic bacteria like *Trueperella pyogenes* and *Fusobacterium necrophorum* (Brodzki *et al.*, 2014) [6] even after ovulation remain in the uterus enabling continuous growth of bacterial after formation of corpus luteum on the other hand post service pyometra occurs due to *Trichomonas foetus*, a protozoan flagellar in nature colonizes in the uterus. In chronic endometritis related with equine pyometra, infectious agents are isolated like *Streptococcus zooepidemicus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumonia* and *Aspergillus* spp. (Samper *et al.*, 2007) [14].

Poor anus-vulvular conformation (the anus was sunken cranially and was not vertically aligned with the vulva resulting in poor anal to vulvular alignment.) is also predisposing factor for occurrence of pyometra. At the ventral fissure of the vulva faecal material is trapped, which results in ascending infection. Urine pooling and wind sucking are mainly responsible factors for the progression of equine pyometra. (Knottenbelt *et al.*, 2003) [10].

Pathogenesis

Mixed populations of bacteria are found in the uterus during the puerperal stage. For several days their numbers constantly increase. Pathogenic microorganisms are removed from the uterus of a typical cow throughout the interim period (up to the first postpartum ovulation). Uterus in favourable conditions, bacteria get established in utero. The uterine environment during the luteal phase is favourable for both microbial growth and pregnancy. Progesterone promotes cervical closure, increased secretion, the expansion and multiplication of endometrial glands, and the inhibition of myometrial contractions. Additionally, the uterine resistance to bacterial infection and the local leukocyte response decline. (Wijewardana *et al.*, 2015) [36]. Estrogen and progesterone levels in the blood are typically excessively high in pyometra, and it is thought that more hormone receptors and their sensitivity will cause an exaggerated response. (Chaffaux S and Thibier M 1978, Prapaiwan N *et al.*, 2017) [7, 24]. Simultaneous corpus luteum and the presence of follicular cysts in animals with pyometra is more common, demonstrating a synergistic hormonal action. (Strom Holst B *et al.*, 2001) [33].

development of endometrial glands, pathologic proliferation, and cyst formation driven by progesterone (i.e. cystic endometrial hyperplasia [CEH]) is also believed to predispose the animal to pyometra.

In case of cattle in chronic cases of pyometra destruction of the endometrium and undergoes fibrotic of uterine wall changes occur and in some severe cases complete recovery and conception cannot occur. In mares affected with pyometra Transluminal adhesions, fibrosis, inelasticity, and other problems are frequently present in the cervix. Mares' regular cyclic behaviour may be maintained or interrupted. The discharge from the genital tract may be absent or only occur during estrous cycles. (Robert O. Gilbert, 2016) [29]. In does Acute endometritis and pyometra often co-occur because of difficult labour and the retained placenta that goes along with it. (Noakes *et al.*, 2008) [23]. In caprine Pyometra is characterized by accumulation of mucopurulent matter or pus

inside uterus (Roberts *et al.*, 1986) [30].

Symptoms

Symptoms of pyometra includes persistent or irregular vaginal discharge with purulent or mucopurulent exudates. While in some cases closed cervix and no any discharge is present. cyclic activity in cows, may present at irregular interval and longer time persistence of corpus luteum for. But cyclicity in mare remain normal, and no any deviation from normal cyclic activity of ovaries is observed. Uterus may feel like 60-120 days of pregnancy on rectal palpation. thick uterine wall can be felt. And doughy. No any signs of pregnancy like presence of foetal membrane slip, unilateral bulging of uterine horns and fremitus present. Systemic signs include fever, anorexia, Decrease milk production. In bitches systemic signs includes anorexia, depression/lethargy, tachycardia, polydipsia, Stachypnea, polyuria, abnormal visible mucous membranes. (Børresen 1979 and Jitpean *et al.*, 2017) [5, 16-17] dehydration, Fever, abdominal pain on palpation, vomiting, anorexia, diarrhoea and gait abnormalities are found in bitches with the disease (Hagman 2018). In goats Postpartum pus is thick mucoid and creamy and yellow or greenish-grey colour. Mucopurulent exudates also observed. (Jainudeen and Hafez, 1987) [15].

Classification of Pyometra

Pyometra can be classified in two types; Depending on the state of the cervix, there are two types of pyometra: open-cervix and closed-cervix. (Verstegen *et al.*, 2008) [34]. It is known as open cervix pyometra when the cervix is open and the diseased material or purulent discharge can exit the body. It is safer and easier to treat. The another one is closed type where fully closed cervix is felt and there will be no discharge from the vulva. It is called closed cervix pyometra, Because there is no uterine drainage in closed-cervix pyometra, the uterus may burst and pus may leak into the abdomen, leading to peritonitis, systemic toxemia, and possibly a quick demise. (Jitpean *et al.*, 2017) [16-17].

Diagnosis

The very first step of diagnosis includes the anamnesis. History taking includes animal age, insemination date, after 21-40 days of insemination animal come in heat if not conceived, cyclic abnormality etc. Purulent or mucopurulent vaginal discharge, an enlarged abdomen, dullness, anorexia, and reduced milk production are all symptoms of pyometra.

Even though there is up to 60 litres of exudate in the uterine canal, a mare with pyometra rarely exhibits overt indications of systemic disease; very rarely, there is weight loss, depression, anorexia, or recurring colic (Noakes *et al.*, 2008) [23]. One peculiar character in mare is that Neither the anus nor the vulva were vertically oriented. (England 2005) [11].

In case of does cervix is relaxed in most cases of postpartum pyometra the and When the doe defecates or lies down, some pus occasionally escapes and is visible. The pus is typically thick, mucoid, creamy, yellow or greenish-grey in colour. (Jainudeen and Hafez, 1987) [15]. After taking history next step of diagnosis is physical examination of animal. In large animals i.e. cattle and buffaloes on per rectal examination uterus feels like 60-120 days of pregnancy with persistent corpus luteum. Uterine wall becomes thick and absence of positive signs of pregnancy like fremitus, uterine caruncles, foetal membrane slip etc. On squeezing the uterine horns pus comes out through vagina if it is open pyometra. Particularly

in the closed-cervix variant of pyometra, where no pus is visible, diagnosis can occasionally be challenging. In such cases other diagnostic methods like radiography, ultrasonography and various other laboratory diagnostic tools can be applied. In cattle Corpus luteum on the ovary, a buildup of fluid with mixed echo-density in the uterine lumen, and uterine distention on ultrasonography are the hallmarks of pyometra. (Manns *et al.*, 1985) [20]. In contrary ultrasonographic examination of mare's genital tract shows snowy appearance of uterus with thickening of uterine wall (Wolfgang, 2004) [18].

Ultrasonographic imaging show tubular organs that are swollen and hypoechoic and contain echogenic fluid, but occasionally pus displays a sluggish, whirlpool-like pattern. Pregnancy, particularly in the pre-mineralization period (less than 45 days), can occasionally be misdiagnosed using an X-ray as a technique of observation. (Pretzer, 2008) [26]. One of the best diagnostic tools is ultrasound imaging, which shows the uterus as an inflated, hypoechoic tubular organ filled with echogenic fluid. Nonetheless, pus can occasionally have a sluggish, whirlpool-like pattern.

Differential Diagnosis

Most of the cases pyometra follows a retained placenta and postpartum metritis, in which case there is frequently an intermittent discharge of pus from the vagina. In pyometra the uterine walls are usually thick and heavy and lack tone. The fluid in the uterus may be watery, syrup-like or viscous. Pyometra should be differentially diagnosed with pseudo pregnancy and pregnancy.

Pseudo pregnancy is commonly found in bitch, mare goat, rabbit etc. In case of pyometra uterine wall usually feels thicker on rectal palpation than normal, uterine tone changes to doughy, absence of fremitus, foetal membrane slip and uterine caruncles while in case of pregnancy uterine wall feels usually thinner on rectal palpation, uterus feels like thick rubber balloon, presence of fremitus, uterine caruncles and allantoichrion foetal membrane slip.

Treatment

administration of PGF2 α . Is common treatment followed. Uterine defense mechanisms is stimulated by treatment of endometritis with PGF2 or a synthetic analogue to disrupt the corpus luteum and removing the progesterone source.

Regardless of the underlying reason, the goal of treating pyometra is to force the corpus luteum to regress, enlarge the ovaries, trigger a protracted contraction of the uterus, and cause the pus to discharge. Pyometra cases are treated either by medicinal treatment or by surgical intervention. Medicinal treatment includes hormonal therapy with estradiol valerate @ 3-10 mg total dose intramuscularly followed by giving the myometrium 20-40 IU of oxytocin 24 hours later in order to sensitise it and dilate the cervix. Most or all of the pus is often evacuated out of the uterus within 24 to 72 hours following treatment. Another therapy includes combination of estrogen and glucocorticoids. Where oestrogen alone has failed to provide excellent results, the use of oestradiol valerate (10 mg or 1 ml. I/M) followed by dexamethasone (5 ml. I/M) has produced good results. Estradiol has been suggested to promote mucus formation, phagocytosis, and myometrium contractions. (Roberts, 1986) [30] and also cause decrease in progesterone concentration. PGF2 α analogues like Dinoprost trometamol @ 20-25mg [Lutalyse (5 ml I/M), Dinoprost (2 ml I/M), and Cloprostenol sodium @ 500 g [Ovuprost] are the

best treatments for pyometra. Within 5-7 days, these result in the regression of the corpus luteum, dilation of the cervix, and pus expulsion. In cattle PGF2 or one of its equivalents administered at regular luteolytic dosages is the preferred course of treatment. In about 80% of cases that are treated, exudate is expelled and the uterus is cleared of bacteria. The majority of cows can be predicted to conceive within three or four inseminations, even though the first-service conception rate following therapy may be low. In 20% of cows, the therapy might need to be repeated. PGF2 (Estrumate) and Iugol's iodine intrauterine infusion were successful in treating postpartum pyometra in does in ewes and does, which may be connected to PGF2's ability to increase uterus contraction with quick evacuation of contents and lower uterine infection. (Al-Hamedawi 2011) [1]. Parenteral antibiotics should be given during the hormonal therapy because the contraction of the uterus reduces the risk of infection spreading to the oviducts. Penicillin (10-40 lakh IU) for 3-5 days can be utilised if an antibacterial medication needs to be pumped into the uterine lumen after pus has been expelled. Additionally useful are other antibiotics like tetracyclines or ampicillin. Aqueous iodine solution 1: 2000 + 30 millimole of lactic acid to every 12 ounces of solution can be used to treat pyometra caused by trichomoniasis. Until the animal enters estrus spontaneously and the discharge stops, the uterus is irrigated once a week. Usually, this necessitates two or three treatments. The uterus is once more irrigated a week after the animal returns to estrus, but the lactic acid is not included in the iodine solution this time. When the discharge has stopped and two typical estrus cycles have passed, treated animals are deemed suitable for breeding. If the endometrium has not undergone significant pathological changes, the animals' chances of becoming pregnant are regarded as fair. In case of canines and felines subcutaneous administration of PGF2 at the rate of 150 μ g/kg/day for more than 10 days showed 100% results (Myhre, 2016) [21], which could be because PGF2 stimulates luteolysis, which blocks progesterone (Renton *et al.*, 1993) [28]. Another treatment using cloprostenol (@ 1 Pg/kg once daily) and cabergoline (@ 5 Pg/kg PO once daily) for seven days was well received. However, progesterone blockers like mifepristone (Hoffman and Schuler, 2000) [13] or aglepristone (Wehrend and Traschbostedt, 2003; Arnold *et al.*, 2006) [35, 2] have recently proven to be a more effective treatment option. Additionally, Contri *et al.* (2015) [9] had success with a strategy that coupled aglepristone with an antibiotic cover that lasted only six days. Another current treatment method for pyometra involves giving acyline, a third-generation GnRH antagonist, orally (single dose), along with amoxicillin-clavulanate, twice daily, orally for seven days.

If medical treatment fails to respond than one should go for surgical treatment. Spaying (ovariohysterectomy) is one surgical procedure for therapy. Spaying effectively and quickly eliminates the infection, avoids uterine rupture and peritonitis, and, of course, stops the disease from returning. Pyometra does occur very infrequently in spayed animals. again although there may be postpartum complications like stump pyometra. Currently, ovariohysterectomy is thought to be the most efficient and secure method of treating pyometra. The afflicted horse uterus may be nearly impossible to drain. Large volumes of fluid should be used to lavage the uterus; however, the condition frequently returns, necessitating hysterectomy or wedge cervix resection to allow continuous uterine drainage, a salvage procedure that keeps the mare in

use but makes her infertile.

After treatment and pus expulsion from the uterus and the establishment of normal estrous cycles the cows should not be rebred for several normal estrous periods. Before breeding is permitted the uterus became normal in size and consistency and no metritis or cervicitis should be present. The use of antibiotic infusions or other therapy as described under endometritis may be of some value in hastening recovery.

Prognosis

Compared to cases that have been present for 120 days or more, those cases that have only been present for 60 to 120 days are more likely to heal and become pregnant. Long-term endometrial destruction and fibrotic alterations to the uterine wall can lead to permanent infertility. (Roberts, 1986) ^[30]. Despite making the mare infertile, pyometra rarely has an impact on the mare's general health and wellbeing. (Noakes *et al.*, 2008) ^[23].

Prevention

Good sanitation and controlled breeding programmes help in prevention of pyometra. Only young bulls that have never been exposed to trichomoniasis should breed with virgin heifers. Through examination physically before breeding should be done of infected bulls and should be culled from the herd. Artificial insemination should be done by experts and semen should be contamination free.

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