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Medical Management of Canine Pyometra

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Abstract:- The present investigation aimed to analyse reproductive issues in dogs with a history of pyometra at the Veterinary Clinical Complex of Nagpur Veterinary College, Nagpur, and private veterinary clinics during the period from April 2022 to July 2023. Pyometra, a reproductive condition affecting approximately 25% of female dogs before the age of ten, is most prevalent in intact, diastral bitches. Specifically, it involves the accumulation of pus within the uterine lumen, typically occurring during or shortly after a period of progesterone dominance. There are two types of pyometra: closed cervix and open cervix. Closed cervix pyometra is particularly hazardous. The most commonly isolated pathogen from pyometra is E. coli. Despite the advancements in medical care, pyometra still carries a 4% fatality rate.

I. INTRODUCTION

Elevated mortality rates are observed in non-addressed instances of canine pyometra, the prevalent reproductive ailment (Singh et al., 2010), characterized by an acute or chronic polysystemic diestrual condition influenced by hormonal factors. Around 18% of all maiden female dogs receive an investigation of this health status before reaching the age of around 9 (Jitpean et al., 2012). Almost one-fourth of femme canines experience the situation before the age of 11 (Egenvall et al., 2001), significantly impacting the virility of canines intended for pedigree reproduction purposes. The disease's spreading mechanism of pyometra involves oestradiol-incited impetus of the uterus, followed by prolonged periods of progesterone supremacy (Sugiura et al., 2004). This leads to a hike in endometrium solidity, enhanced endometrial secretion outputs, and a reduction in uterine myocyte curtailments due to progestin influence. In a progestin-primed womb, the suppression of WBCs and neutrophils facilitates infection proliferation. The enterobacterium stands out as the primary causative agent responsible for canine pyometra (Chen et al., 2003). Among gram-negative microbes, especially E. coli, is the utmost frequently found causative factor from pyometra-affected uteri.

Gram-negative bacteria toxin, a potent initiator of inflammatory reaction is generated by bacterial toxin and exempts within the circulatory system over microbial growth and demise (Hagman and Greko et al., 2005). Medically, pyometra can be categorized as either closed (absence of vaginal discharge) or open cervix pyometra (accompanied by vaginal transudate). Patients with closed cervix pyometra face an elevated risk of developing septicemia and toxaemia, potentially leading to a fatal outcome if left untreated (Smith, 2006). Common symptoms of pyometra encompass lethargy, depression, appetite loss, frequent urination and defecation, nausea, vomiting, and diarrhoea. Pyometra is commonly associated with tiredness, dullness, loss of appetite, frequent urine and bowel movements, nausea, vomiting, and diarrhoea. The identification of pyometra is based on deviation in the blood tests such as mild normocytic, normochromic, non-regenerative anaemia and leukocytosis with absolute neutrophilia, which causes a degenerative left shift (Baithalu et al., 2010). According to Baithalu et al. (2010), the medical signs of canine pyometra typically encompass a degenerative left shift, toxic neutrophils, and peripheral leukocytosis that frequently exceeds 40,000 cells/mm^3. The presence of mild normocytic normochromic non-regenerative anemia suggests that the condition is persistent. notably often used indicators of renal values are raised blood urea nitrogen (BUN) or serum creatinine values, which signify kidney damage or inadequacy (Jurka et al., 2010). Diagnostic methodologies for pyometra include ultrasonography and abdominal palpation, revealing a palpably enlarged uterus. Gastrointestinal examination and imaging are two screening techniques for pyometra that show an evidently swollen womb.

The sonogram features of pyometra can differ greatly from case to case based on the level of infective potential and the makeup of the contents (Pande 2001). The fluoro and enro antibiotics were shown to be the most effective therapy for canines with pyometra by analysis of isolates and susceptibility; Aminoglycosides were the next most effective treatments (Pande, 2001). Relying on the condition of the womb and the overall health of the female dog, medical intervention for pyometra involving agents that promote the expulsion of uterine pus, along with antimicrobials, is a viable option in specific situations (Gobello et al., 2003). Prostaglandins (PGF2) have been traditionally recommended by physicians for treating pyometra in females (Gilbert et al., 1999). Treatment side effects that are often experienced include dyspnea, nausea, diarrhoea, and increased salivation. Promising results have been seen when a new regimen incorporating the antiprogestin aglepristone with only six days of antimicrobial therapy is administered (Contri et al., 2014). Diminutive doses of the substances that prevent the synthesis of prolactin cabergoline and a synthetic dinoprost

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analogue (cloprostenol) have been utilized to regale pyometra in bitches, yielding positive results (Ahmed et al., 2015). Misoprostol has been proven to be a secure and reliable therapy for pyometra. Its combination with dinoprost introduces propitious remedial possibilities for the effective control of any sort of pyometra (Shah et al., 2016). A standardised and efficient treatment for pyometra has not yet been developed, although the quick advances in veterinarian pharmaceutical science, pathology investigation, and invention (Kumar and Saxena 2018).

II. MATERIAL AND METHOD

In present study, total twenty four clinical cases of the dogs with case record of pyometra presented at the Veterinary government college medical facility, Nagpur Veterinary College Nagpur from April 2022 to July 2023. The primary objective of the current investigation were to assess the treatment response to dogs affected with pyometra to antiprogesterone and PGF2α therapy and to check their efficiency.

➢ *Treatment*

The pyometric dogs presented to Nagpur veterinary college, Nagpur at TVCC were subjected at random to any of the following three treatments along with supportive therapy as follows:

- Class I (N = 8):Natural prostaglandin Dinoprost Tromethamine (Inj Lutalyse, 10ml each ml contain 5 mg Dinoprost Tromethamine, Zoetis India Limited, Mumbai, India) was administered subcutaneously @ 0.2 mg/kg b.wt. b.i.d for Six days.
- Class II (N = 8): Mifeprex (Mifegest Kit each kit containing one tablet of mifepristone 200mg, Zydus Healthcare Limited, East Sikkim, India) was administered @ 2.6 mg/kg b.wt. orally b.i.d from six days .
- Class III (N = 8): Treatment given was Mifeprex @ 2.6 mg/kg b.i.dorally upto six days along with prostaglandin F2 alpha tromethamine subcutaneously @ 0.3 mg/kg b.wt. on alternative days i.e. days First, third and Sixth.

III. RESULTS AND DISCUSSION

The current investigation was planned to assess how well canines with pyometra responding to anti progestin and Dinoprost tromethamine medication and to check their efficiency. Retrospective study was done to record the important reproductive issues in canine having history of pyometra, presented at Nagpur veterinary college TVCC, Nagpur from April 2022 to July 2023. The case records were studied and classified under appropriate condition of reproduction.

Table 1 Signalment in 24 Cases of Canine Pyometra

Case No.	Age (Years)	Breed	Last estrus	Mating in last estrus	Parity
1.	3	Bull mastiff	74	-	M
2.	4	Saint Bernard	120	-	N
3.	8	Labrador	N.K.	-	P
4.	4.5	Labrador	N.K.	-	N
5.	8	Saint Bernard	60	-	P
6.	10	Labrador	10	+	M
7.	1	Tibetan Mastiff	30	+	N
8.	3	Pitbull	20	+	N
9.	8	Pomeranian	150	+	N
10.	5	Cross Breed	30	-	N
11.	10	Pomeranian	N.K.	-	N
12.	9	Pug	60	-	N
13.	1.5	Pug	N.K	-	P
14.	6	Rottweiler	45	-	N
15.	1	Dalmatian	30	-	N
16.	2	Pitbull	60	-	N
17.	7	Pug	30	-	N
18.	8	Pomeranian	N.K.	-	N
19.	1.5	Siberian Husky	45	+	N
20	4.5	Pug	120	-	N
21.	1.5	Pitbull	120	-	N
22.	2.5	Pitbull	45	+	M
23.	3	Shih Tzu	45	+	N
24.	5	ND	40	+	N

N.K. = Not known; P = Primiparous; N = Nulliparous; M = Multiparous

➢ *Bacteriological Findings*

The prevalent bacterial isolates identified in twenty four therapeutic instances of pyometra in canines are detailed in Table 2 and Figure 1 of the current investigation.

Pyometra-affected canines' vaginal samples were cultured and found to contain E. coli in 58.33 percent, Staphylococcus sp. in 25 percent, Klebsiella sp. in 12.5 percent, and Pseudomonas sp. in 4.1 percent. The

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bacteriologic analysis of 24 vaginal samples obtained from canines affected by pyometra indicated that Escherichia coli predominated. These findings agree with those that Dhaliwal et al. (1998) described, who identified E. coli as the primary causative agent of pyometra. Additionally, Klebsiella sp., Streptococci sp., Staphylococci sp., and the anaerobic bacteria Pseudomonas sp. were identified as the causative agents. According to Bondade *et al.* (2010), E. coli is the prevailing bacterium responsible for pyometra. Hagman (2012) additionally documented that E. coli emerged as the primary pathogen in dog pyometra, accounting for around 70% of the cases. Furthermore, the virulence factors associated with particular strains of the etiological coli included the capability to attach itself to certain endometrial targets.

Table 2 Bacteriological Examination of Vaginal Swabs from Pyometra Affected Dogs

Bacterial identified	Total samples	Percentage
E. Coli	14	58.33%
Staphylococcus sp.	6	25%
Klebsiella sp.	3	12.5%
Pseudomonas sp.	1	4.1%

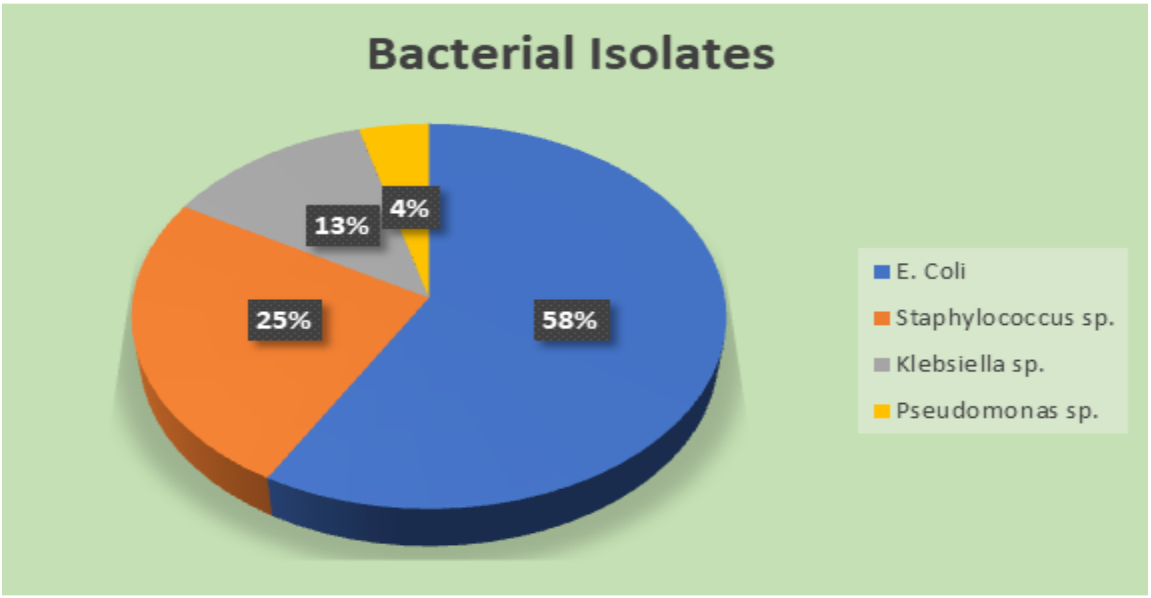

Fig 1 Oranisms Isolates on Culture of Vaginal Discharge

The antimicrobial susceptibility of the cultures was evaluated against gram-negative (Table 3) and gram-positive (Table 4) bacteria.

Considering the range of inhibition's length, the cultures were categorized as either sensitive or resistant. The gentamicin exhibited the highest sensitivity (87.50%) towards gram negative bacteria, followed by amikacin (83.33%) and tobramycin (72.73%). The pharmaceuticals enrofloxacin (61.11%), cefotaxime (58.33%), kanamycin (70%), sulfadiazine (55.56%), neomycin (60%) and norfloxacin (55.56%) exhibited sensitivity levels ranging from 50 to 70%. A minimum of 50% of the samples exhibited sensitivity to streptomycin (22.22%), amoxicillin (20%), and tetracycline (44.44%). Pencillin G exhibited a resistance of one hundred percent in vitro.The antibiotics with the highest sensitivity (100%) in cultures derived from gram-positive bacteria were gentamicin and tobramycin, with cefotaxime following suit (80%).

The sensitivity of the following pharmaceuticals was determined to be as follows: 60% for enrofloxacin, 40% for sulfadiazine, 20% for streptomycin. Pencillin G exhibited a resistance of one hundred percent in vitro. These outcomes align reflect the findings of Bassessar et al. (2013), who discovered that the sensitivity of E. coli isolates was one hundred percent to gentamicin, seventy-five percent to enrofloxacin, sixty-five percent to ciprofloxacin, and fifty-five percent to amoxicillin. One hundred percent of the organisms exhibited resistance to oxytetracycline and tetracycline. The Staphylococcus sp. isolates exhibited the highest efficacy (100%) towards enrofloxacin, followed by gentamicin, erythromycin, amoxicillin, and chloramphenicol (each at 65%). Conversely, the remaining antibiotics proved to be ineffectual against the acquired isolates. In contrast to the findings of Verstegen *et. al.*, (2008), which indicated that Aminopenicillins, Aminopenicillins plus Beta-lactamase Inhibitors , cephalosporins, and intensified sulfonamides exhibited greater sensitivity, the present study demonstrates that amoxicillin and cephalosporins have a high resistivity. According to Robaj *et. al.*, (2016), the frequent utilization of ampicillin and penicillin in veterinary medicine to treat severe infections in canines could potentially contribute to the development of resistance to these antibiotics. Bacteria that cause persistent infections, such as Pyometra, frequently integrate nosocomial resistance plasmids, rendering them more challenging to control, as stated by Chang *et. al.*, (2014).

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Table 3 Antimicrobial Sensitive/Resistance of Gram-Negative Bacteria (E. Coli,Klebsiella sp., Pseudomonas sp.) in Pyometra Affected Dogs

Antibiotics	Sensitive (%)	Resistance (%)
Enrofloxacin	61.11	38.89
Gentamicin	87.50	12.50
Amikacin	83.33	16.67
Tobramycin	72.73	27.27
Kanamycin	70	30
Cefotaxime	58.33	41.67
Neomycin	60	40
Sulfadiazine	55.56	54.44
Norfloxacin	55.56	44.44
Tetracycline	44.44	55.56
Amoxicillin	20	80
Streptomycin	22.22	77.78
Penicillin G	0	100

Table 4 Antimicrobial Sensitive/Resistance of Gram-Positive Bacteria(Staphylococcus sp.) in Pyometra Affected Dogs

Antibiotic	Sensitive(%)	Resistance(%)
Enrofloxacin	60	40
Gentamicin	100	0
Tobramycin	100	0
Cefotaxime	80	20
Sulfadiazine	60	40
Tetracycline	40	60
Streptomycin	20	80
Penicillin G	0	100

➢ *Treatment*

Three distinct medicinal interventions were applied to twenty-four canines with pyometra.

- *Class I*

Dogs numbered 1-8 comprised Group I(Table 5). These dogs were treated with Dinoprost Tromethamine (Inj Lutalyse) @ 0.1 mg/kg b.wt. subcutaneously b.i.dfor 5 days alongwith antibiotic Enrofloxacin (Floxidin™ Vet) @ 6 mg/kg b.wt. intramuscularly b.i.dfor 6 days. Seven out of eight dogs responded to the treatment with disappearance of clinical signs viz. lethargy, inappetence and vaginal discharge. The dog's overall well-being heals and its hunger returns once the pus is expelled from the female reproductive organ (Tainturier and Treboz 1985). Animal number three did not respond to the treatment and vaginal discharge continued.Owing to the condition, the dog was ovariohysterectomized and recovered successfully thereafter.

- *Class II*

Animal numbered 9-16 comprised Group II(Table 5). These dogs were treated with Mifepristone (Mifegest Kit) @ 2.6 mg/kg b.wt. orally b.i.dfor 6 days along with antibiotic Enrofloxacin @ 6 mg/kg b.wt. b.i.d. intramuscularly for 6 days. All the animals responded well to the treatment. There was absence of discharge after the treatment and all the animals were active. However, the animal no. 10 after recovery was subjected to ovariohysterectomy owing to the owner's wish.

- *Group III*

Animal numbered 17-24 comprised Group III(Table 5). These dogs were treated with Misoprostol @ 2.6 mg/kg b.i.d orally for upto 6 days along with PGF2 alpha THAM subcutaneously @ 0.3 mg/kg b.wt. on alternate days i.e. days 1, 3 and 5 along with the antibiotic Enrofloxacin @ 6 mg/kg b.wt. b.i.d. intramuscularly for 6 days. All the animals responded well to the treatment except one animal in which discharge continued after treatment. The dog was ovariohysterectomized and recovered successfully thereafter.

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Table 5 Response of Different Treatment in Pyometra Affected Dogs

Groups	Case No.	Treatment response	Long term response
Group I (Dinoprost tromethamine)	1.	Recovered	Recovered but died later
	2.	Recovered	Recovered but died later
	3.	OVH	-
	4.	Recovered	Recovery (No estrus)
	5.	Recovered	Recovery (No estrus)
	6.	Recovered	-
	7.	Recovered	Recovery (No estrus)
	8.	Recovered	Recovery (No estrus)
Group II (Mifepristone)	1.	Recovered	Recovery (No estrus)
	2.	Recovered	OVH at owner request
	3.	Recovered	Recovery (No estrus)
	4.	Recovered	Recovery (No estrus)
	5.	Recovered	-
	6.	Recovered	Recovery (No estrus)
	7.	Recovered	-
	8.	Recovered	Recovery (No estrus)
Group III (Mifepristone + Dinoprost tromethamine)	1.	Recovered	Recovery (No estrus)
	2.	Recovered	Recovery (No estrus)
	3.	OVH	-
	4.	Recovered	-
	5.	Recovered	Recovery (No estrus)
	6.	Recovered	Recovery (Estrus after 2 month)
	7.	Recovered	Estrus after 3 months, animal whelped
	8.	Recovered	Recovery (No estrus)

Following the conclusion of therapy, TLC values declined significantly ($P<0.05$) in each group. After the therapy was finished, the percentage of neutrophils in each group was significantly ($P<0.05$) lower than the values before the start of the therapy. These results are consistent with those of Jena et al. (2013b), who observed that PGF2α therapy resulted in a rise in Hb and a decrease in TLC and neutrophil %. A comparable investigation by Bigliardi et al. (2004) found that, in comparison to utilising medical intervention alone, treating mild cases of cystic endometrium hyperplasia with PGF2αand antibiotics frequently had positive effects. Wehrend et al. in 2003 also observed that leukocytosis restored to the typical physiological level following the effective therapy of closed cervix pyometra with antiprogestin on days 1, 2, and 7.

Shah et al (2016) also reported that in pyometra affected dogs' TLC and neutrophil percent returned to their normal level after treatment. Therapeutic plans' effects on blood biochemical measurements. The average initial BUN levels were 29.4 ± 10.64, 20.43 ± 6.24 and 30.63 ± 5.53 mg/dL in the three groups respectively with a range of 6-123 mg/dL. At the time of recommendation, BUN was determined to be more than 40 mg/dl in five dogs. The BUN levels of the remaining animals were all within normal range. All of the canines in this research responded well to medicinal therapy.

IV. CONCLUSION

Based on above observations, following conclusions were drawn from the present study:

- The disease was most common in middle aged animals during diestrus stage. However, younger animals less than 2 years of age were also susceptible to pyometra.
- Nulliparous animals had a higher susceptibility to danger. The occurrence of the illness was seen in animals that had previously given birth after mating during their following estrus cycle, maybe due to infection resulting from unsanitary conditions.
- Escherichia coli was identified as the predominant bacterium responsible for pyometra in dogs. Among the antibiotics tested, Gentamicin had the highest level of sensitivity (>80%) against this bacterium, whereas Enrofloxacin shown a sensitivity of 60%.
- All the therapies offered shown equivalent efficacy in the resolution of pyometra in the canine subjects. Nevertheless, the dogs that were treated just with PGF2α or mifepristone did not exhibit any observed estrus activity. Hence, the use of a combination therapy including mifepristone and PGF2α may be seen a more favorable approach for the management of pyometra, since it has shown the ability to induce estrus and facilitate conception.

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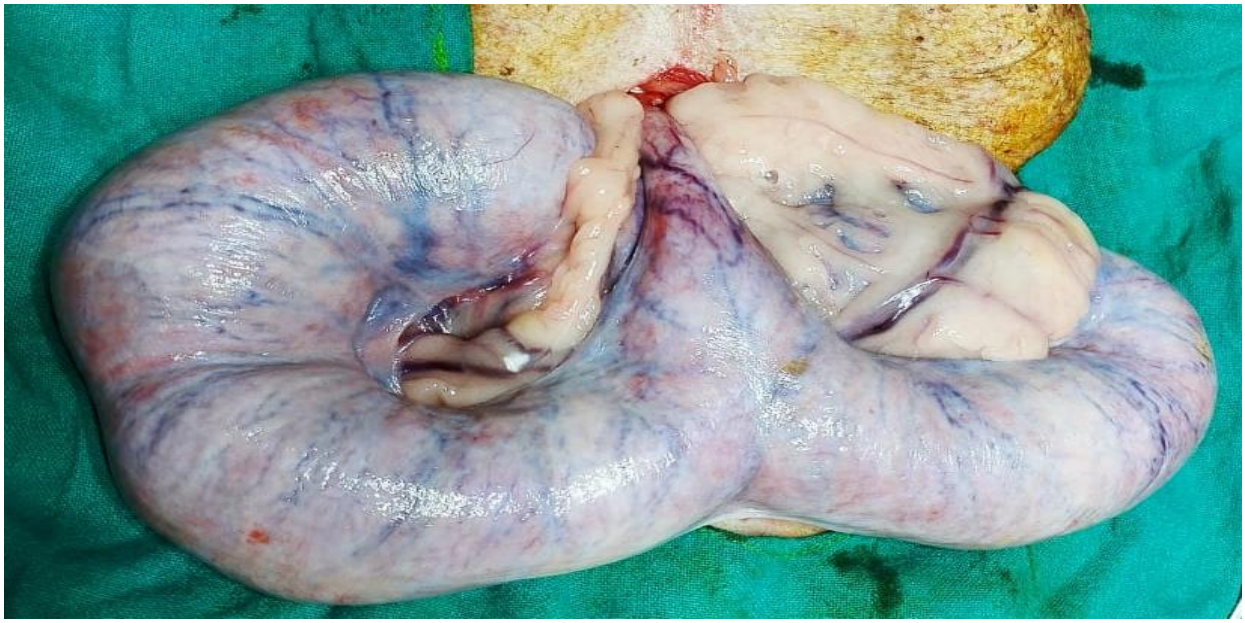
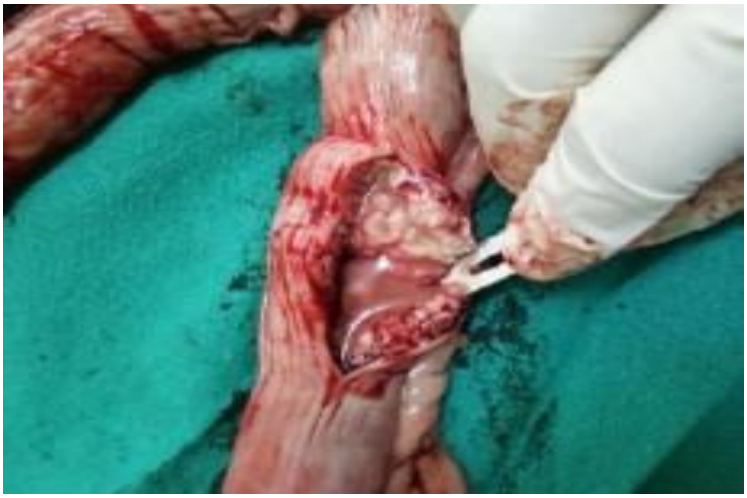


Fig 2 Gross Appearance of Pyometra



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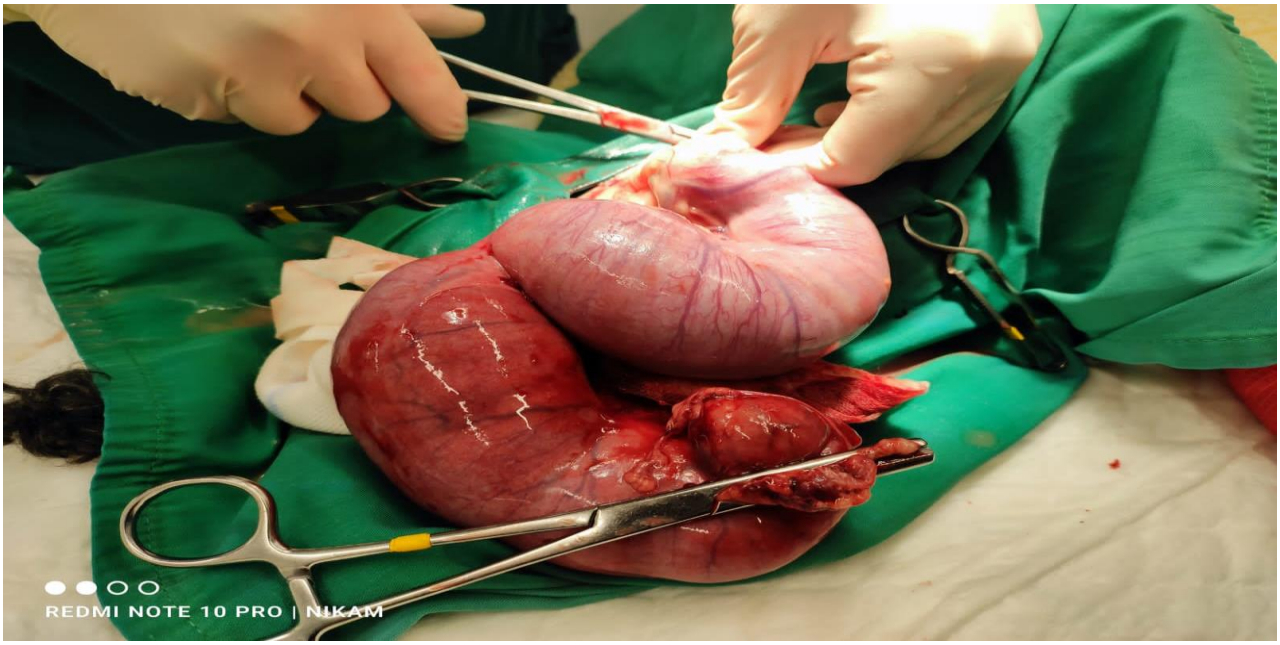

Fig 4 Ligation of Uterine Horn

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