



Hematological and Biochemical Findings in Juvenile Queens Diagnosed with Pyometra

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Pyometra is an acute or chronic suppurative inflammation of the uterus, primarily observed in older animals. Delayed diagnosis and progression of the disease significantly increase mortality rates. Moreover, biochemical changes in queens with pyometra are generally ambiguous, and hematological abnormalities are mostly absent. In mild cases, no detectable changes may be observed. Queens are known for their meticulous grooming behavior, which can obscure clinical signs. Additionally, as pyometra is more commonly associated with older animals, suspicion of the condition in juvenile individuals is often overlooked. This study investigates cases of pyometra diagnosed in juvenile queens, particularly in those that have never given birth. The animal material of the study comprised 20 juvenile queens in total, including 10 healthy juvenile queens and 10 juvenile queens diagnosed with pyometra. Hemogram and biochemical parameters were evaluated from blood samples collected from the animals. According to the complete blood count, the white blood cell (WBC), hematocrit (HCT), and mean corpuscular volume (MCV) values of the pyometra queens were found to be increased, while the monocyte (MON) value was decreased ($p<0.05$). The alkaline phosphatase (ALP) levels in the pyometra queens were found to be decreased ($p<0.05$). In conclusion, while pyometra is generally considered a disease of middle-aged and older queens, it can also occur in young queens. Early diagnosis and ovariohysterectomy are effective in restoring health in affected queens. Further studies involving larger sample sizes and diverse breeds of young queens with pyometra are recommended to provide more comprehensive and meaningful insights.

Key Words: Anesthesia, juvenile queens, ovariohysterectomy, uterine infection

Piyometra Tanısı Konulan Genç Kedilerde Hematolojik ve Biyokimyasal Bulgular

Piyometra, genellikle yaşlı hayvanlarda görülen, uterusun akut veya kronik süpüratif yangısıdır. Tanının geç konulması ve hastalığın ilerlemesi ölüm oranlarını önemli ölçüde artırmaktadır. Ayrıca, piyometralı dişi kedilerde biyokimyasal değişiklikler genellikle belirsizdir ve hematolojik anormallikler çoğunlukla görülmeyebilmektedir. Hastalığın çok ilerlemediği vakalarda, tespit edilebilir hiçbir değişiklik gözlenmeyebilir. Kedilerin sürekli kendini temizlemesi klinik bulguları gizleyebilmektedir. Ayrıca, piyometra daha çok yaşlı hayvanlarla ilişkilendirildiğinden, genç kedilerde bu durum göz ardı edilmektedir. Bu çalışmada, özellikle hiç doğum yapmamış ve piyometra teşhisi konulan genç kediler incelenmiştir. Çalışmanın hayvan materyalini, 10 sağlıklı ve 10 piyometra teşhisi konulan toplam 20 genç kedi oluşturmaktadır. Sağlıklı ve piyometra teşhisi konulan genç kedilerden toplanan kan örneklerinden, hemogram ve biyokimyasal parametreler değerlendirilmiştir. Tam kan sayımına göre, piyometralı genç kedilerin beyaz kan hücreleri (WBC), hematokrit (HCT) ve ortalama eritrosit hacmi (MCV) değerleri yüksek, monosit (MON) değeri ise düşük bulunmuştur ($p<0.05$). Ayrıca piyometralı kedilerin alkalen fosfataz (ALP) seviyelerinin düştüğü tespit edildi ($p<0.05$). Sonuç olarak, piyometra genellikle orta yaşlı ve yaşlı kedilerin hastalığı olarak kabul edilse de, genç kedilerde de görülebilmektedir. Erken teşhis ve ovariohisterektomi yapılarak, piyometralı genç kediler sağlığına kavuşabilir. İleride yapılacak çalışmalarda hayvan sayısının artırılması ile daha kapsamlı ve anlamlı sonuçlar elde edilebilir.

Anahtar Kelimeler: Anestezi, genç kedi, ovariohisterektomi, uterus enfeksiyonu

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Introduction

The cystic endometrial hyperplasia-pyometra complex is an acute and chronic suppurative inflammation of the uterus (1). The disease is most commonly observed in animals aged 4 to 7 years (2). Pathogens causing pyometra account for 25% of diseases in unspayed queens under the age of 10 (3). The mortality rate of the disease is reported to range between 5.7% and 8% (4, 5).

Queens are seasonal polyestrous animals that enter anestrus during the winter season. Their estrus period typically lasts 6–7 days. Ovulation can occur either by induction or, rarely, spontaneously. In queens where ovulation occurs but pregnancy does not follow, a diestrus or pseudopregnancy phase lasting approximately 40 days is observed. During this period, progesterone is secreted at basal levels. The increase in progesterone weakens the uterine defense mechanism, making it more susceptible to bacterial infections (6). Various pathogens, including *Escherichia coli*, *Streptococcus spp.*, *Staphylococcus spp.*, and *Klebsiella spp.*, are frequently isolated in pyometra cases (7). Among these, *E. coli* strains play a dominant role, and the release of bacterial endotoxins into systemic circulation can lead to severe complications such as endotoxemia, septic shock, and death (6).

Symptoms of pyometra can vary depending on the openness of the cervix, the presence of endotoxemia, secondary bacterial infections, the severity of the disease, and its duration (8, 9). Peritonitis is the most common complication in pyometra. Due to the risk of severe complications such as septicemia, azotemia, endotoxemia, uterine rupture, shock, and peritonitis, it should be considered an emergency case (10). The most commonly observed symptoms include increased abdominal volume, anorexia, vaginal discharge, lethargy, depression, vomiting, abdominal distension, and shock characterized by abnormal fever (4, 8, 11, 12). Vaginal discharge can vary from sanguineous to mucopurulent or even severe bleeding (3, 13, 14). Due to queens grooming habits, detection of vaginal discharge may be delayed (12, 15). Additionally, polyuria and polydipsia are generally not reported in queens. Most of the time clinical signs are mild or faint in queens with pyometra (11, 16). Clinical signs related to the disease may also affect the bladder and kidneys in addition to the uterus (17).

Biochemical changes in queens with pyometra are less pronounced compared to dogs. It is common for queens to not exhibit hematological abnormalities. In cases of sepsis, hyperproteinemia, hypokalemia, azotemia and increased levels of alanine aminotransferase (ALT) and alkaline phosphatase (ALP), blood urea nitrogen (BUN) and creatinine (CRE) may be seen. It is also quite common for no changes to be detected in mild cases (11).

Pyometra is typically observed in queens over 3 years of age that have not given birth or in those over 5 years old that have given birth. Additionally, due to their continuous grooming habits, vaginal discharge may go unnoticed in queens. Since the disease is more commonly seen in older queens, the suspicion of pyometra may be overlooked in juvenile individuals. Recently, the risk of pyometra in juvenile queens has become a significant concern. This study specifically investigates cases of pyometra diagnosed in juvenile queens that have never given birth. In this context, the hematological and biochemical parameters of queens diagnosed with pyometra at a juvenile age have been examined.

Materials and Methods

Research and Publication Ethics: This study was conducted at Van Yuzuncu Yil University Animal Hospital. This research was approved by Van Yuzuncu Yil University Animal Experiments Local Ethics Committee with a document that does not require approval for experimental animals (Date: 26/12/2024; Decision No: 2024/12-31).

Animals: The animal material of the study consisted of a total of 20 juvenile queens, aged 8 to 14 months and weighing between 2.4 and 3.9 kg, with 10 healthy juvenile queens and 10 juvenile queens diagnosed with pyometra. In addition, when planning the trial design of the study, it was determined that 20 animals were sufficient according to the results of the

power analysis. According to the information obtained from the owners, no treatment had been applied to suppress estrus in the juvenile queens. Informed consent forms were obtained from the owners of all the animals. The diagnosis of pyometra was made based on history, clinical findings, and ultrasound examination. Clinical signs included polyuria, polydipsia, anorexia, lethargy, vaginal discharge, and fever. Juvenile queens that came for routine examination and did not have any health problems constituted the control group of the study.

Blood Samples: Blood samples from healthy and pyometra-affected young queens were collected from the cephalic vein (*V. cephalica*) during the initial examination into both anticoagulant-containing (1 mL) and anticoagulant-free (3 mL) tubes. Hemogram and biochemical parameters were evaluated from the collected blood samples. For biochemical analysis, the blood samples were centrifuged at 3000×g for 10 minutes (Nüve NF-200) to obtain serum. The serum samples were analyzed using a biochemical analyzer (Randox, Monaco, UK), while the hemogram was assessed directly from whole blood using a hemogram analyzer (Diatron MI Ltd, Hungary). Hemogram parameters assessed included white blood cells (WBC), neutrophils (NEU), monocytes (MON), lymphocytes (Lym), red blood cells (RBC), hemoglobin (Hgb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and platelets (PLT). Biochemically, BUN, CRE, ALT, AST, ALP, total bilirubin, and total protein (TP) levels were investigated.

Surgical Treatment: Ovariohysterectomy (OHE) was performed on juvenile queens diagnosed with pyometra. OHE was performed under inhalation anesthesia. Butorphanol (Butomidor® Wels, Austria, 0.3 mg/kg) for premedication, Propofol (Propofol-PF®; Tekirdağ, Türkiye, 4 mg/kg, IV) for induction. Isoflurane (Isoflurane USP®; Piramal Critical Care, Inc, Bethlehem, ABD, 0.5-2%) for maintenance of anesthesia. Amoxicillin-clavulanic acid (Synulox®; Latine, Italy, 12.5 mg/kg, SC, BW) orally twice daily for 5 more days after the operation. For analgesia at home, cats received meloxicam (Metacam®; Mexico, Mexican, orally 0.2 mg/kg BW first day, followed by 0.1 mg/kg BW second day).

Histopathological Examination: The uterus tissue samples were fixed in a 10% buffered formaldehyde solution and embedded in paraffin blocks after routine follow-up, and 4 µm sections were taken with a microtome. Normal slides were used for Hematoxylin and Eosin (H&E) staining. Sections were examined under a light microscope and photographed.

Statistical Analysis: Data were performed using SPSS 21 statistical software. The data were evaluated using the Kolmogorov-Smirnov test and found to be normally distributed. Independent Samples T-test was used to assess the differences between the groups. Variables were expressed as mean±standard error of the mean (SEM) values. $p < 0.05$ values were accepted for the significance level of the tests. Post hoc power

analysis was carried out using the G*Power tool (version 3.1.9.7; Universities of Düsseldorf, Mannheim and Kiel, Germany) to determine the study's sample size. Post hoc power analysis results (effect size=0.30, $\alpha=0.05$ and $1-\beta=0.80$) revealed that 20 animals would be needed for the sample size.

Results

According to the information obtained from the owners, none of the queens died postoperatively. Most of the queens with pyometra exhibited symptoms such as anorexia, polyuria, polydipsia, and lethargy. The average age of the queens with pyometra was 11.1 months, and their average weight was 3.2 kg. The majority of the queens were of mixed breed (50%). Among the queens diagnosed with pyometra, 4 had no history of mating, vaginal stimulation, or exogenous hormone use. Eight queens had open-cervix pyometra, while 2 had closed-cervix pyometra.

Histopathological evaluations revealed the presence of corpus luteum in all ovarian tissue samples and significant pathological changes in the uterine

tissue. Severe hemorrhage in the endometrium, accompanied by abundant neutrophil infiltration in the uterine lumen, was observed. Additionally, multifocal cystic endometrial hyperplasia was identified. Neutrophil infiltration within the lumens of the endometrial glands and pronounced hemorrhagic areas were noted. Hyperplasia of glandular epithelial cells was observed, along with neutrophil infiltration in the glands and multifocal hemorrhagic areas in the endometrium. These findings demonstrate the simultaneous occurrence of inflammation and hyperplasia in the uterine tissue, leading to significant histopathological alterations (Figure 1).

The complete blood count for juvenile queens with pyometra is presented in Table 1. According to the complete blood count, the WBC (27.50 ± 4.39), HCT (63.34 ± 28.73), and MCV (75.81 ± 34.81) values of the pyometra queens were found to be increased, while the MONO (4.17 ± 0.31) value was decreased ($p<0.05$). The biochemical results are summarized in Table 2. Biochemically, the ALP levels in the pyometra queens were found to be decreased ($p<0.05$).

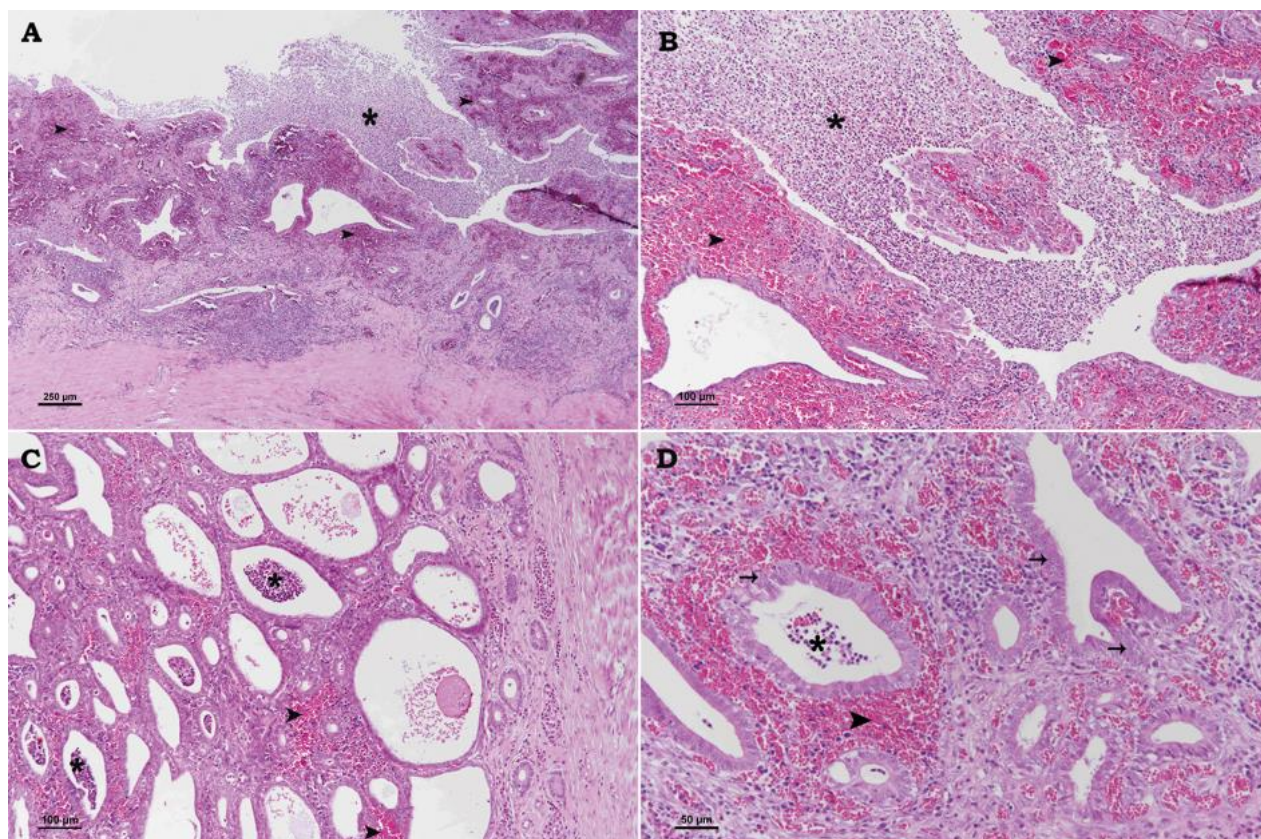


Figure 1. Histopathological changes in uterine tissue. A) There is abundant neutrophil leukocyte infiltration (*) in the uterine lumen and severe hemorrhage (arrowhead) in the endometrium. HE, Scale bar = 250 μm . B) Close-up view of Image A. HE, Scale bar = 100 μm . C) Multifocal cystic endometrial hyperplasia is observed. Neutrophil leukocyte infiltrate the lumens of the endometrial glands (*) and endometrial hemorrhage (arrowhead) are shown. HE, Scale bar = 100 μm . D) Hyperplasia of gland epithelial cells (arrows) and neutrophil infiltration in the glands (*) and multifocal endometrial haemorrhage (arrowhead) are shown. HE, Scale bar = 50 μm

Table 1. Complete blood count results of control and pyometra-diagnosed juvenile queens groups (mean±SEM)

Parameters	Control Group (n=10)	Pyometra Group (n=10)	p Value
WBC (10 ⁹ /L)	9.27±0.94	27.50±4.39	0.003
NEU (%)	58.13±3.55	73.55±3.49	0.888
MON (%)	4.89±0.55	4.17±0.31	0.042
LYM (%)	32.57±4.18	18.03±2.94	0.235
RBC 10 ¹² /L	9.64±0.27	8.33±0.61	0.205
HGB (g/dL)	12.72±0.49	11.21±0.78	0.282
HCT (%)	37.69±1.28	63.34±28.73	0.049
MCV (fl)	39.11±0.89	75.81±34.81	0.044
MCH (pg)	12.18±1.08	13.36±0.43	0.330
PLT (10 ⁹ /L)	328.70±48.07	251.00±46.89	0.775

* Complete blood count (CBC), white blood cell (WBC), neutrophils (NEU), monocyte (MON), lymphocyte (Lym), red blood cell (RBC), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelets (PLT).

Table 2. Serum biochemical analysis results of control and pyometra-diagnosed juvenile queens groups (mean±SEM)

Parameters	Control Group (n=10)	Pyometra Group (n=10)	p value
BUN (mg/dL)	30.94±7.84	54.78±7.33	0.631
CRE (mg/dl)	1.31±0.10	1.16±0.12	0.875
ALT (U/L)	45.95±5.33	94.43±12.41	0.055
AST (U/L)	29.09±3.42	77.17±9.14	0.094
ALP (U/L)	35.00±7.37	29.40±3.03	0.014
TBIL (mg/dL)	0.73±0.59	0.47±0.07	0.073
TP (g/dL)	7.22±0.22	7.94±0.26	0.808
Glucose (mg/dL)	207.64±95.39	128.57±13.60	0.083

* Blood urea nitrogen (BUN), creatinine (CRE), alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (TBIL), total protein (TP).

Discussion

Queens are seasonally polyestrous and often exhibit induced ovulation, which results in less exposure to progesterone. Therefore, pyometra is less commonly observed in queens. Since the clinical signs of pyometra are usually unnoticed in queens, the disease can progress to advanced stages before a diagnosis is made. A delayed diagnosis of pyometra can be dangerous and life-threatening (5, 18-20). Although there are numerous studies on pyometra, it is noteworthy that most of these studies have been conducted on bitches. In contrast, there is a need for studies focusing on pyometra in queens. The reproductive physiology of bitches and queens differs significantly. Notably, there is a lack of studies in the literature regarding pyometra in juvenile queens. The present study evaluates the blood biochemical and

hematological results of juvenile queens diagnosed with pyometra.

Pyometra is typically a disease of middle-aged or older animals. As age increases, the risk of pyometra also increases. A significant rise is observed in cats older than 7 years (21, 22). In another study, pyometra was reported to occur at an average age of around 4 years (5). In present study, the ages of the queens diagnosed with pyometra ranged from 8 to 18 months. This indicates that pyometra can occur even in very young queens. The mortality rate of the disease is reported to be around 3-4% in dogs (21), whereas in cats, it is between 5.7-8% (4, 5). It has been suggested that this discrepancy may be due to queens being less sensitive to endotoxins, or clinical signs being less pronounced unless sepsis develops (18, 23). Mild clinical signs of the disease can lead to disease progression and potentially negative outcomes (4). However, if the uterus ruptures and septic peritonitis develops, the mortality rate can rise to 31-57%. Therefore, delayed diagnosis of pyometra makes the disease dangerous and life-threatening (18-20). In present study, no uterine rupture was found during the surgery of the queens. Additionally, it was learned from the pet owners that none of the queens died after the operation. This may have been due to early diagnosis and intervention.

The reference range for WBC in healthy queens is 5.5-19.5×10⁹/L (24). As in pyometra, increased bacterial density of the uterus causes an increase in WBC (25). Neutrophils are the most common type of white blood cell in the body and play a crucial role in fighting infections. Therefore, the increase in WBC is associated with neutrophils. In the presence of pyometra, an increase in the number of immature neutrophils leads to an increase in WBC (26). Studies have shown that in bitches and queens with pyometra, neutrophilic leukocytosis can be observed in the complete blood count (26), although in some cases, no changes may be seen in the complete blood count in queens (6). In queens diagnosed with Pyometra, WBC and granulocyte levels increased, while lymphocyte levels decreased (27). In the present study, the WBC levels of juvenile queens with pyometra were significantly increased. Although the increase in neutrophils was not statistically significant, there was a substantial increase proportionally. Additionally, although there was no significant difference in lymphocyte levels, a proportional decrease was observed. All of these findings support the study of Satilmis (27). In bitches with pyometra, an increase in leukocyte count and lymphocytopenia have been reported to be directly associated to the severity of the disease. Furthermore, in bitches, progesterone has been associated with immunosuppression and endotoxemia, which leads to a decrease in lymphocyte levels (28, 29). In present study, the proportional decrease in lymphocyte count and the proportional increase in neutrophil count could be attributed to the immunosuppressive effects of progesterone and uterine endotoxins.

Pyometra is a chronic inflammatory disease, and as a result, moderate normocytic, normochromic, non-regenerative anemia often develops. Chronic blood loss can lead to the development of microcytic hypochromic anemia (30, 31). In bitches with pyometra, anemia is typically explained by the passage of erythrocytes through diapidesis into the uterus, bone marrow suppression, and vaginal discharge (32, 33). In a study by Nak et al. (31), normocytic normochromic anemia developed in dogs. In the present study, it was observed that while MCH levels did not change, MCV levels were increased. This situation can be medically defined as macrocytic anemia. In a study conducted in queens, it was reported that anemia did not develop in pyometra queens and RBC, MCV and MCH levels remained within the reference range. Furthermore, HCT levels were found to be increased due to dehydration (27). In the present study, the lack of change in RBC and the significant increase in HCT in the pyometra group supports the findings of Satilmis (27).

In queens and bitches with pyometra, significant increases in BUN and creatinine levels have been reported in pyometral dogs (27, 29). These parameters are directly related to renal function, and their increase indicates renal dysfunction. Consequently, it is reported that prognosis can be negatively affected (4). In pyometra cases, the increase in CRE and BUN values has been linked to stress, shock, toxemia, and nephropathy resulting from the accumulation of purulent content in the uterine lumen (34). One other study found that serum CRE and BUN values remained within reference ranges when prerenal azotemia due to dehydration did not develop (26). There is limited information available about kidney damage in cats with

pyometra. Unlike dogs, biochemical parameters in cats are not specific for the diagnosis of pyometra (11). In present study, while there was a proportional increase in BUN levels in queens with pyometra, statistically, the BUN and creatinine levels were similar to those in the healthy group. This might be explained by the fact that the majority of queens in the pyometra group had open-cervix pyometra. In queens diagnosed with pyometra, hyperproteinemia, hypokalemia, azotemia, and increased liver enzymes (AST and ALP) may be observed, particularly in cases accompanied by sepsis and dehydration (11). However, in our study, there was no significant difference in TBIL and TP levels. Additionally, ALT and AST levels were similar to the healthy group, while the ALP level was significantly lower.

In conclusion, although pyometra is typically a disease of middle-aged and older queens, it has been increasingly observed in juvenile queens in recent years. Future studies could investigate the incidence of pyometra in juvenile queens. The clinical signs of the disease may not be severe in the early stages, or the disease may be overlooked because cats frequently groom themselves. Early diagnosis and OHE can restore health in affected cats. Anemia and leukocytosis are common findings in infectious diseases. Additionally, increased levels of ALT, AST, ALP, urea, and creatinine can be observed in many internal problems. In the present study, although there was a proportional increase in ALT, AST, and BUN values, these did not reach statistically significant levels. We believe that future studies on young cats with pyometra, with a larger sample size and involving different breeds, may yield more meaningful results.

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