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Evaluation of the prevalence of Systolic hypertension in Persian cats with poly cystic kidney disease

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ABSTRACT

Polycystic kidney disease (PKD) is a genetic disorder prevalent in Persian and Persian-related cat breeds. It often leads to systemic arterial hypertension, which can severely affect the kidneys and heart if not managed. This study aimed to assess the prevalence of hypertension in Persian cats with PKD. Conducted at Tehran Azma Veterinary Center from March to May 2023, the research included 24 cats of Persian or Persian-mixed breeds. The cats were divided into two groups based on kidney ultrasonography examinations: a control group and a PKD group, each containing 12 cats. Systolic blood pressure was measured using Doppler ultrasonography and categorized according to the guidelines of the International Renal Interest Society (IRIS). The mean kidney size in cats with PKD was found to be significantly larger than that in the control group (p < 0.05). The average blood pressure of the PKD cats was substantially higher, recorded at 165.0 ± 23.5 mm Hg, with a higher mean in azotemic cats. The study found that 75% of the PKD cats had hypertension, with 25% experiencing severe hypertension, putting them at a high risk of future organ failure. In conclusion, hypertension is highly prevalent in Persian cats with PKD, and the progression of PKD, along with the presence of azotemia, can impact systolic blood pressure. Therefore, proactive strategies and hypertension management should be considered in PKD cats.

ارزیابی شیوع فشار خون سیستولیک در گربه های ایرانی مبتلا به بیماری کلیه پلی کیستیک نیلوفر صابری ^۱، احسان خاکسار ^۲*، محمد ملازم ^۳، سیامک مشهدی *ر*فیعی ^۱

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چکیدہ

بیماری کلیه پلی کیستیک (PKD) یک اختلال ژنتیکی شایع در گربه های نژاد پرشین و گربه های مخلوط با پرشین است. این بیماری اغلب منجر به افزایش فشار خون شریانی سیستمیک می شود، که در صورت عدم کنترل می تواند منجر به آسیب بر کلیه ها و قلب شود. هدف از این مطالعه بررسی میزان شیوع فشار خون بالا در گربه های پرشین مبتلا به PKD بود. این پژوهش از اسفند تا اردیبهشت ۱۴۰۱ در مرکز دامپزشکی تهران آزما انجام شد، شام ۲۴ گربه از نژاد پرشین و مخلوط با پرشین بود، که براساس معاینات سونوگرافی کلیه به دو گروه تقسیم شدند : گروه کنترل و گروه کنترل و گروه شامل ۲۲ گربه بود. فشار خون سیستولیک با استفاده از سونوگرافی داپلر اندازه گیری شد و تنایج بر اساس راهنمای انجمن بین المللی علاقمند به کلیه (IRIS) طبقه بندی شد. میانگین اندازه کلیه در گربه های PKD به طور قابل توجهی بزرگتر از گروه کنترل بود (۵۰-۹ میانگین فشار خون در گربههای PKD با ساس راهنمای انجمن بین المللی علاقمند به کلیه (IRIS) طبقه بندی شد. میانگین اندازه کلیه در گربه های PKD به طور قابل توجهی بزرگتر از گروه کنترل بود (۵۰-۹ میانگین فشار خون در گربههای PKD با دامنه ای از ۱۳۰ تا ۲۰ میلیمتر جیوه، به طور قابل توجهی در مقایسه با گروه کنترل بالاتر بود. این مطاله نشان داد که ۲۵٪ از گربه های PKD هشار خون بالا داشتند و ۲۵٪ فشار خون در گربه های PKD بسیار شایع استرا بود تا ۲۰ میلیمتر جیوه، به طور قابل توجهی در مقایسه با گروه کنترل بالاتر بود. این مطاله نشان داد که ۲۵٪ از گربه های PKD هشار خون بالا داشتند و ۲۵٪ فشار خون شدید را تجربه کردند، که آنها را در معرض خطر بالای نارسایی اندام های آینده قرار می دهد. در نتیجه، فشار خون بالا در گربه های ایرانی مبتلا به گره ته گره استو و پیشرفت PKD همراه با وجود آزوتمی می تواند بر فشار خون سیستولیک تأثیر بگذاری استراتژی های پیشگیرانه و مدیریت فشار خون بالا بای در فلر مع بالا به از می ایندام های آینده قرار خون بالا در نور مود رفتر گرفته شود. با وجود آزوتمی می تواند بر فشار خون سیستولیک تأثیر بایل ایند ما مو مدیریت فشار خون بالا باید در گربه های طر گرفته شود.

واژه های کلیدی: گربه های پرشین، بیماری کلیه پلی کیستیک ، فشار خون بالای سیستولی، شیوع، سونوگرافی داپلر

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INTRODUCTION

Polycystic kidney disease (PKD) is a hereditary condition characterized by the gradual formation of fluid-filled cysts in the kidneys and, occasionally, in other organs like the liver and pancreas [1]. In felines, this condition is notably widespread, particularly among Persian cats, making it one of the most common genetic disorders in this breed, alongside diabetes and feline lower urinary tract disease [1]. Nevertheless, the Persian breed is not the only one impacted by this condition. Other breeds, including the Exotic Shorthair, Himalayan, British Shorthair, American Shorthair, Burmilla, Ragdoll, Maine Coon, Neva Masquerade, and Chartreux breeds, can also be susceptible to this pathology [1, 2]. The global occurrence of PKD in Persian and Persian-related cats is around 38%, with variations ranging from 36% to 49.2%. In Iran, the estimated prevalence of PKD in Persian and Persian-related cats is reported to be 36.8% [3]. This hereditary condition. transmitted through autosomal dominance, stands as one of the most prevalent genetic diseases in humans, identified as Autosomal Dominant Polycystic Kidney Disease (ADPKD) [4]. The condition results from mutations in either the PKD1 or PKD2 gene, with the former being more prevalent, accounting for 85% of cases, while the latter is responsible for the remaining instances [5]. The occurrence of polycystic kidney disease (PKD) in felines is linked to a genetic mutation in the PKD1 gene [6]. Cysts may develop as outpouchings from various segments of the nephron, leading to the gradual deterioration of parenchyma renal [1]. If the clinical manifestations, whether renal or extra-renal, are not addressed, this condition advances to endstage renal disorder [5, 7]. The preferred diagnostic approaches for identifying Polycystic Kidney Disease involve imaging (PKD) examinations, particularly ultrasound, along with newly developed genetic analysis techniques [1, 8, 9]. Ultrasonography can identify cysts in felines as young as 7 weeks old [10]. High blood pressure is prevalent among individuals with ADPKD, with occurrences exceeding 70% even before the onset of renal dysfunction is apparent [11]. The mechanisms underlying the development of high blood pressure (BP) in ADPKD, especially during the early stages of the disease, remain incompletely understood. Two primary theories offer potential explanations for the pathogenesis of hypertension in ADPKD. One theory suggests inherent cardiovascular dysfunction linked to abnormal ciliary and vascular function, resulting in elevated blood pressure. Another theory posits that the cystic kidney contributes to intrarenal ischemia, activating the reninangiotensin-aldosterone system (RAAS) and causing an increase in BP. Additionally, several studies have reported the activation of the sympathetic nervous system (SNS) as a contributing factor [5, 11, 12]. High blood pressure can lead to left ventricular hypertrophy (LVH) and is recognized as a significant risk factor for cardiovascular-related mortality [13], [14]. Unregulated high blood pressure can accelerate the decline of kidney function [15]. Certain studies indicate that elevated blood pressure may expedite cyst growth [11, 15]. It becomes crucial to initiate prompt and efficient hypertension treatments early on to reduce the adverse impact on the health and survival of patients with ADPKD [15]. Given the limited knowledge in this area for felines, the objective of this study is to assess the incidence of systolic hypertension in Persian cats affected by polycystic kidney disease. As Persian cats trace their origins to Iran, it is noteworthy to explore the considerable prevalence of polycystic kidney disease (PKD) in this region. Understanding the implications of PKD, including potential consequences such as hypertension, is essential for clinicians in

effectively managing the adverse effects of the disease. Given the limited knowledge in this specific area concerning felines, the objective of this study is to assess the incidence of systolic hypertension in Persian cats affected by polycystic kidney disease.

MATERIALS AND METHODS

The study commenced with physical examinations conducted on 68 male and female Persian and Persian-mixed cats referred to Tehran Azma Veterinary Center from March to May 2023, all of which possessed a normal body condition score [16]. Various clinical signs, including anorexia, fever, vomiting, diarrhea, dyspnea, cough, seizure, cyanosis, exercise intolerance, edema, and ascites, were considered. Cats exhibiting any of these signs were excluded from the survey. Following the physical examinations, abdominal ultrasound scans were performed on 57 Persian and Persian-related cats. The cats, positioned in dorsal recumbency, underwent the examination using a diagnostic ultrasound machine from Mindray, China, equipped with a linear and micro-convex transducer (7.5-12 MHz). The cats were awake and restrained by their owners. A positive diagnosis for PKD was assigned if one anechoic cavity was found in any of the kidneys [17] (Figure 1). Cats displaying any abnormalities on their abdominal ultrasound scans were eliminated from the study. Among the animals, 21.05% (n=12) were diagnosed with PKD through abdominal ultrasonography. For the control group, 12 Persian and Persianrelated cats with no evidence of systemic disease and no kidney cysts were randomly selected (Figure 2). Systolic blood pressure (SBP) measurements were acquired for each group through Doppler ultrasonography (Vet-Dop2, Vet Quip, Australia). Cats were situated in a calm environment for 5-20 minutes prior to

the measurement to alleviate anxiety. The cuff was affixed to the right forelimb, and the probe was positioned on the first palmar common digital artery. Cats were permitted to sit in their preferred position. The average of five consecutive measurements was regarded as the SBP in cats [18, 19]. The Persian cats were categorized as normotensive, prehypertensive, hypertensive, and severely hypertensive based on the International Renal Interest Society (IRIS) guideline [20].

Statistical analyses were performed using SPSS software version 26.0. Descriptive statistics, such as mean \pm SD, median, minimummaximum, frequency, and percentage, were utilized. Following this, the normality of the data was assessed using the Kolmogorov-Smirnov test. Differences among variables were evaluated through Pearson Chi-Square, Fisher's exact tests, Mann-Whitney, and independent T-tests. A p-value less than 0.05 was considered statistically significant.

RESULTS

The research involved 24 Persian cats, with an equal distribution of 12 (50%) males and 12 (50%) females. No notable distinctions in gender were observed between PKD and non-PKD cats (p=0.436). The mean age of the overall cat population was 60 ± 30.84 months, ranging from 12 to 144 months. Within the PKD group, the mean age was 59 ± 26.32 months (ranging from 24 to 96 months), while in the non-PKD group, it was 61 ± 35.98 months (ranging from 12 to 144 months). No significant difference in age was observed between the two groups (p = 0.563) (Table 1). The average body weight of the 24 Persian cats included in the study was 4.25 ± 0.93 kg, with a range from 2.75 to 5.90 kg. Among PKD cats, the mean body weight was 4.24 ± 0.94 kg (ranging from

2.75 to 5.85 kg), while for non-PKD cats, it was 4.27 ± 0.95 kg (ranging from 2.90 to 5.90 kg). However, these values did not show a significant difference (p = 0.937) (Table 1). The average body weight of the 24 Persian cats included in the study was 4.25 ± 0.93 kg, with a range from 2.75 to 5.90 kg. Among PKD cats, the mean body weight was 4.24 ± 0.94 kg (ranging from 2.75 to 5.85 kg), while for non-PKD cats, it was 4.27 ± 0.95 kg (ranging from 2.90 to 5.90 kg). However, these values did not show a significant difference (p = 0.937) (Table 1). The mean kidney size of cats with PKD was 4.12 ± 0.6 cm (range: 3.4–4.6 cm). In contrast, the control group exhibited a mean kidney size of 3.42 ± 0.6 cm (range: 3.1-4.3 cm), which showed a significant difference (p = 0.017).

Additionally, the mean cyst size within the kidneys of Persian cats with PKD was 6.51 \pm 11.5 mm (range: 2.5–25 mm) (Table 1). Although the blood pressure remained within the normal range for all cats in the control group, 16.66% (n=2) of these cats were prehypertensive. In contrast, hypertension was detected in 75% (n=9) of cats with polycystic kidney disease (PKD), with 25% (n=3) classified severely hypertensive. as Additionally, prehypertensive blood pressure was noted in 16.66% (n=2) of PKD-afflicted cats, while only 8.33% (n=1) of the PKD population exhibited normal systolic blood pressure (Table 2).



Figure 1: Normal kidney ultrasonography image of the Persian cat enrolled in the study. The kidney is oval or bean-shaped, with a smooth outline, well-defined, and with a normal size. The length of the kidney is illustrated by a dotted line (Dist: 4.33 cm), indicating the cortex (1) and medulla (2).



Figure 2: ultrasonography image of a cyst in the kidney of the Persian cat enrolled in the study. The cyst in the cortex of the kidney is demonstrated by the yellow arrow.



Figure 3: Mean systolic blood pressure of Persian cats enrolled in the study.

SBP=Systolic Blood Pressure

Table 1. The mean age, weight, and kidney size of the cats enrolled in this study

| Parameters | PKD cats (n=12) | Non-PKD cats (n=12) | p value |
|-------------|--|---|---------|
| Age | 59 ± 26.32 months (24 - 96 months) | 61 ± 35.98 months (12 - 144 months) | 0.563 |
| Weight | 4.24 ± 0.94 kg (2.75 - 5.85 kg) | $4.27 \pm 0.95 \text{ kg} (2.90 - 5.90 \text{ kg})$ | 0.937 |
| Kidney size | 4.12 ± 0.6 cm (3.4–4.6 cm) | 3.42 ± 0.6 cm (3.1–4.3 cm) | 0.017 |

Table 2. The prevalence of hypertension of Persian cats enrolled in the study (based on IRIS blood pressure substages guideline

| Systolic blood pressure | PKD cats (n=12) | Non-PKD cats (n=12) |
|---------------------------|-----------------|---------------------|
| substage mmHg | | |
| Normotensive<140 | 8.33% | 83.33% |
| Prehypertensive 140-159 | 16.66% | 16.66% |
| Hypertensive 160-179 | 50% | 0% |
| Severely hypertensive>180 | 25% | 0% |

Regarding systolic blood pressure, a noteworthy distinction was noted between the groups with and without polycystic kidney disease (PKD) ($p \le 0.001$). The average systolic blood pressure in cats without PKD was 127.5 ± 7.50 mm Hg (ranging from 120 to 140 mm Hg), whereas in cats with PKD, it measured 165.0 ± 23.5 mm Hg (ranging from 130 to 220 mm Hg) (figure 3). Furthermore, there was a statistically significant difference in the mean SBP between Azotemic PKD cats, with a mean of 182.0 ± 22.8 mm Hg (range: 160-220), and non-Azotemic PKD cats, with a mean of 152.8 ± 16.0 mm Hg (range: 160-170) ($p \le 0.001$) (Figure 3). Although the blood pressure remained within

the normal range for all cats in the control group, 16.66% (n=2) of these cats were prehypertensive. In contrast, hypertension was detected in 75% (n=9) of cats with polycystic disease (PKD), with kidney 25% (n=3) classified as severely hypertensive. Additionally, prehypertensive blood pressure was noted in 16.66% (n=2) of PKD-afflicted cats, while only 8.33% (n=1) of the PKD population exhibited normal systolic blood pressure (Table 2).

DISCUSSION

Conducting epidemiological studies and assessing prevalence, along with early detection

of hypertension in cats with PKD, is a crucial strategy for controlling and managing the consequences of hypertension. Consequently, it is strongly advised to implement a screening program for the early identification of hypertension in cats with PKD. Polycystic Kidney Disease (PKD) is recognized as a chronic kidney disease. CKD is commonly identified alongside hypertension, indicating a complex cause-and-effect relationship between the two conditions. It is recommended that, upon diagnosing CKD in cats, a comprehensive evaluation for the presence of hypertension should be conducted. This proactive approach ensures a thorough understanding of the feline patient's health, allowing for timely and effective management of both CKD and any associated hypertension [21]. Examining the link between indirect blood pressure and systemic hypertension in different stages of CKD in cats, the study categorized diseased cats according to the International Renal Interest Society (IRIS) guidelines into stages II and III-IV. The findings unveiled an elevated risk of severe hypertension in cats with CKD, especially in advanced stages. This underscores a potential heightened risk of severe hypertension in feline patients experiencing advanced CKD, emphasizing the crucial need monitoring for vigilant and tailored management in these instances [22]. In our study, we observed a significant influence of disease progression and azotemic status on systolic blood pressure. As the disease progresses, the compromised renal function can result in fluid and electrolyte imbalances, activation of the renin-angiotensin-aldosterone system, and increased sympathetic nervous system activity. These physiological changes contribute to elevated blood pressure. The findings from the investigation conducted on both azotemic and non-azotemic cats unveiled elevated blood pressure levels in the azotemic group when compared to their non-azotemic

counterparts. Moreover, the prevalence of hypertension in the studied population was documented at 38%. [23]. In the present study, it was found that the systolic blood pressure (SBP) of azotemic PKD cats was remarkably higher compared to both the control group and non-azotemic cats. This may be linked to the complex interplay of renal dysfunction, fluidelectrolyte imbalances, and the activation of regulatory systems that influence blood pressure regulation. The average blood pressure values observed in our study for cats with polycystic kidney disease (PKD) surpassed those documented in another clinical study involving clinically healthy cats. In the latter study, blood pressure was measured using the oscillometric method. This discrepancy in blood pressure levels underscores the distinctive nature of blood pressure dynamics in cats afflicted with PKD compared to their clinically healthy counterparts in previous research [24]. Research on cats afflicted with Polycystic Kidney Disease (PKD) has demonstrated an elevated mean atrial pressure in comparison to a control group[25]. The results obtained in our study closely resemble those of the referenced study, indicating a noteworthy similarity in the observed outcomes. In our study, 75% of PKD cats were hypertensive or severely hypertensive. According to the IRIS blood pressure substages, cats experiencing hypertensive and severely hypertensive blood pressure are at a moderate to high risk of future organ damage [20]. In human research, primary manifestation the of Autosomal Dominant Polycystic Kidnev Disease (ADPKD) often begins with Systemic Arterial Hypertension. Studies suggest that the activation of the renin-angiotensin-aldosterone system (RAAS) is a significant factor in the development of hypertension, resulting from cyst expansion and renal ischemia [26]. If left untreated, hypertension can lead to an increase in left ventricular mass, which is linked to heart failure, arrhythmias, cardiovascular mortality,

and adverse renal outcomes [13, 26]. About 60% of individuals with Autosomal Dominant Polycystic Kidney Disease (ADPKD) encounter hypertension as a prominent early indicator, occurring even before any decline in renal function is evident[26]. Patients commonly encounter hypertension as their main symptom, and in contrast to other kidney disorders, a significant proportion of them (approximately 50-70%) exhibit normal kidney function when hypertension first appears [13]. In the present study, despite the clinical normalcy exhibited by PKD cats, there was a noteworthy finding of a 75% prevalence of hypertension among these seemingly asymptomatic feline subjects. This intriguing observation underscores the potential for concealed health risks in cats with PKD, even in the absence of overt clinical abnormalities. The findings from our present study align closely with outcomes observed in prior investigations involving both feline and human subjects. Remarkably, cats afflicted by Polycystic Kidney Disease (PKD) demonstrated a significantly elevated systolic blood pressure (SBP) compared to the control group. The progression of PKD and the presence of azotemia can influence systolic blood pressure. The prevalence of hypertension was particularly striking among cats with PKD, with only a single feline participant in this group displaying normal blood pressure. This solitary instance of normal blood pressure might be attributed to the relatively young age of the cats (12 months) and the early stage of the disease. Contrastingly, within the control group, cats exhibited a prehypertensive stage, which could potentially be attributed to stress factors. This observation underscores the importance of considering environmental stressors when evaluating blood pressure parameters in cats without PKD. The identification of such a high prevalence of hypertension raises questions about the subtleties of disease manifestation and warrants further investigation into the underlying

mechanisms and long-term implications for the health of these feline patients.

CONCLUSION

This study highlights a significant observation, revealing a remarkable prevalence of hypertension in Persian and Persian-related cats diagnosed with PKD at Tehran Azma Veterinary Center. Moreover. а notable PKD percentage of cats demonstrated prehypertensive conditions. The clinical implications of these findings are crucial, emphasizing the importance of vigilant patient monitoring and the implementation of targeted interventions to effectively control hypertension. Recognizing the high prevalence of hypertension in PKD cats, it becomes essential for clinicians to adopt proactive management strategies. These strategies, including early detection and robust hypertension control measures, can significantly mitigate the risk of adverse consequences in Persian cats affected by PKD.

However, to further solidify and expand upon these insights, future research endeavors should prioritize a larger sample size for a more comprehensive understanding of the clinical applications of these findings

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ETHICS

Approved.

CONFLICT OF INTEREST

None.

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