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Short Paper

Prevalence of polycystic kidney disease in Persian and Persian related-cats referred to Small Animal Hospital, University of Tehran, Iran

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Summary

Background: Autosomal-dominant polycystic kidney disease (ADPKD) is the most prevalent inherited genetic disease of cats, predominantly affecting Persians and Persian-related cats. **Aims:** The purpose of this study was to determine prevalence of polycystic kidney disease (PKD) in Persian cats in Iran, and also to assess the relationships between PKD and gender, age as well as clinical and paracilinical manifestations. **Methods:** Sonographic screening examination was performed on all healthy and unhealthy Persian and Persian-related cats referred to Small Animal Hospital of Faculty of Veterinary Medicine, University of Tehran, from April 2014 to May 2015. Cats were classified as positive when at least one anechoic cavity was found in at least one kidney. **Results:** Of 76 Persian and Persian-related cats submitted for PKD ultrasound screening, 36.8% were found to have the disease and 63.2% were negative. Therefore, the prevalence of PKD was estimated 36.8% in Persian and Persian related cats in Tehran, Iran, which is approximately similar to prevalence in other parts of the world. Furthermore, there was a significant correlation between PKD and age, as in affected cats the detection probability of renal cysts in sonography was increased in older animals. For each year increase in age, the detection probability of PKD in sonography was increased about 2.62 times. **Conclusion:** The prevalence of the PKD amongst Persian cats in Iran is relatively high, and insufficient attention to incidence and prevalence of PKD especially in breeding programs, would spread the disease throughout in Persian cats.

Key words: Iran, Persian cat, Polycystic kidney disease, Prevalence, Sonography

Introduction

Polycystic kidney disease (PKD) is a genetic and incurable disorder characterized by abnormal fluid-filled cysts formation in one or both kidneys, remodeling of extracellular matrix, inflammation, and fibrosis formation in the affected kidney (Norman, 2011). Polycystic kidney disease occurs in human and some other animals particularly in cats. There are two main forms of this disease in human: autosomal-dominant polycystic kidney disease (ADPKD) that is the prominent form of PKD in human, and the other form is autosomal recessive polycystic kidney disease (ARPKD) that has a slower rate of disease progression (Iglesias *et al*., 1983). A similar form of ADPKD is identified in Persian and Persian related cats. Polycystic kidney disease is the most prominent inherited feline disease, and affects approximately 6 to 13.8% of cats of variable breeds (Lyons *et al*., 2004; Domanjko-Petric *et al*., 2008). Polycystic kidney disease in Persian and Persian-related cats is an autosomal dominant inheritance disease characterized by renal as well as hepatic and pancreatic cysts that could culminate in chronic renal failure after a variably clinical course. This process is progressive and different from cat to cat, and in some affected animals may lead to end stage renal disease by 3 to 10 years of age (Eaton *et al*., 1997). The prevalence of PKD in Persian and Persian-related cats is approximately 38% worldwide as it ranges between 36% and 49.2% (Barrs *et al*., 2001; Beck and Lavelle, 2001; Cannon *et al*., 2001; Barthez *et al*., 2003; Paryan *et al*., 2016). A genetic mutation in *PKD1* gene is responsible for feline PKD development. In affected animals, a C>A transversion is identified in exon 29, resulting in a stop mutation at position 3284, which suggests a loss of ~25% of the C-terminus of the protein (Lyons *et al*., 2004). As with all inherited diseases, there is not any definite treatment for PKD and so the diagnosis of affected animals and prevention of affected animal breeding are critical factors for control and incidence reduction of this disease in the future. The prevalence of this disease has been estimated in some countries such as USA, Australia, UK, Germany and France, however there are few studies about this disorder in Iran, which is the motherland and origin of

the Persian cat. In the present study, the prevalence of PKD was assessed in Persian and Persian-related cats in Iran, and the relationships between the presence of PKD and gender, age, clinical and paraclinical manifestation were studied.

Materials and Methods

All Persian and Persian-related cats older than 6 months of age submitted to Tehran University Hospital, were included in the present study from April 2014 to May 2015, and younger cats were excluded because of the increased possibility of a false negative result in ultrasonography. Ultrasonography was used to establish or eliminate a diagnosis of PKD in 76 cats in this study. Cats were classified as positive when at least one anechoic cavity was found in at least one kidney (Barthez *et al*., 2003). Cats were restrained by their owners in the awake state or sedated with ketamine (10 mg/kg), administered intramuscularly, and ultrasound examination was performed on cats in dorsal recumbency using a diagnostic ultrasound machine (GE Voluson 730 Pro, Austria) equipped with multifrequency 4-dimensional (4D) linear transducer (6-18 MHz). Also, a complete physical examination, blood cell counts, serum biochemistry tests and urinalysis were performed in each cat. The most important clinical signs considered in the present study were anorexia, polyuria, polydipsia, fever, vomiting, diarrhea and weight loss. The patients were reported as negative or positive for significant clinical signs. Blood cell count was determined using an automatic veterinary hematology cell counter (Nihon Kohden, Celltac Alpha, Tokyo, Japan). The amounts of urea, creatinine, total protein, albumin, aspartate aminotransferase, alanine aminotransferase and glucose were measured by commercial kits (Pars Azmoon, Tehran, Iran), using an autoanalyser (Kone, Finland). Urine specific gravity and urine gamma-glutamyltransferase to creatinine ratio were determined for each patient in random urine samples.

Statistical analysis was conducted using SPSS for windows (release 18, SPSS Inc., Chicago, USA). In addition to descriptive statistics, for data analysis t-test (to compare the hematology and biochemistry changes between cats with PKD and cats without PKD) were performed. Furthermore, the relative contribution of explanatory variables (age, sex and clinical signs) upon the occurrence of the outcome variable (PKD) in the population was determined using binary logistic regression. The independent variables were entered in the model in one single step. A P-value of less than 0.01 was considered significant.

Results

In the present study a total of 76 cats were examined comprising 67 (88.2%) Persians and 9 (11.8%) Persian-related cats. In ultrasonography, PKD was positive in 28 (36.8%) cases, and negative in 48 (63.2%) cases. Figure 1 shows multiple renal fluid-filled cysts of varying size, as spherical and anechoic structures in a Persian cat with PKD. The prevalence of PKD in Persian and Persian-related cats were estimated 38% and 33%, respectively, and the difference was not significant (P>0.01). Of the 76 cats, 34 (44.7%) were male and 42 (55.3%) were female. The prevalence of PKD in male and female cats was 38.2% and 35.7%, respectively, and no sex predilection was identified (odd ratio (OR):1.54, P>0.01). The mean±SD age at presentation for all cats was 2.3 ± 1.38 years (range, 6 months to 12 years), and the mean±SD age of cats diagnosed with PKD was 3.3 ± 1.6 years (range, 1.2 to 11y). The presence of PKD in cats significantly correlated with age (OR: 2.62, confidence interval 1.56-4.33, P<0.01). The results showed that the older the age of the patient, the higher the detection probability of PKD in sonography. For each year increase in age, the detection probability of PKD in sonography was increased about 2.62 times. Bilateral and unilateral polycystic kidneys were 75% (21 out of 28 cases) and 25% (7 out of 28 cases), respectively. Of the 28 cats with PKD, 9 cats (32%) showed renal failure signs and all the patients, with the exception of one patient, died three months after admission. A Persian cat with uremia (Urea: 137 mg/dl and Creatinine 3.7 mg/dl), and mild anorexia survived more than two years. This cat also had a persistent eosinophilia with unknown origin. In the present study, there was not any significant correlation between the presence of PKD and clinical signs (OR: 1.14, P>0.01). Of the 28 cats with PKD, 12 cats (43%) showed at least one significant clinical sign in physical examination (related or not related to renal failure), and of the 48 cats without PKD, 15 cats (31%) were positive for clinical signs. Also, the biochemistry, hematology and urine analysis results were not significantly different between affected and nonaffected animals (P>0.01), (Table 1).

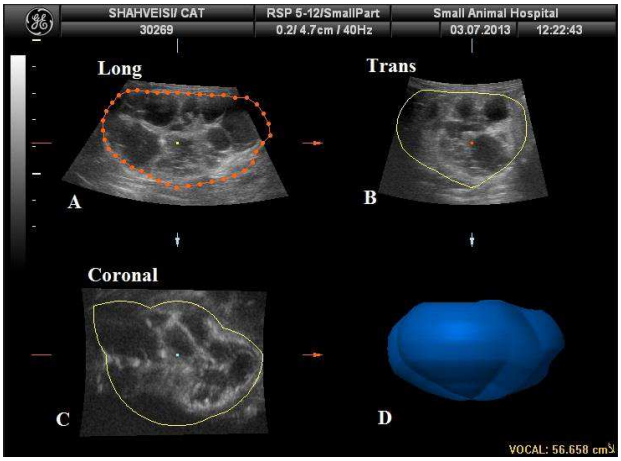

Fig. 1: Ultrasonographic image of a kidney showing multiple fluid-filled cysts of varying size, as spherical and anechoic structures in a Persian cat with ADPKD. A 3D acquisition has been made of the entire polycystic kidney and displayed in three orthogonal planes: longitudinal, transverse, and coronal planes in frames **A**, **B**, and **C**, respectively. Frame **D** shows a 3D inversion mode

Table 1: The comparison of hematology and biochemistry factors between PKD positive and PKD negative cats

Hematology factors (mean±SE)				Biochemistry and urine factors (mean±SE)			
Factor	PKD^+ (28 cats)	PKD^- (48 cats)	Reference range	Factor	PKD^+ (28 cats)	PKD^- (48 cats)	Reference range
WBC	17.27±2.91	17.00±2.07	5.5-19.5×10^{-3}/µL	ALT	82.80±12	66.52±9.76	28-76 IU/L
Neutrophils	68.73±3.34	68.20±4.65	35-75%	AST	60.92±18.10	37.91±4.72	5-55 IU/L
Lymphocytes	20.26±3.14	23.7±3.68	20-55%	GGT	2.84±0.56	3.09±0.80	1-7 IU/L
Hct	35.67±2.06	36.62±1.52	29-45%	ALP	161.14±95	72.68±11	0-62 IU/L
Hg	11.71±0.68	11.79±0.48	9.5-15 g/dl	Urea	93.03±17.13	100.98±26	14-72 mg/dl
RBC	7.18±0.50	7.67±0.33	6-10×10^6/µL	Creatinine	2.64±0.58	2.63±0.74	0.8-2.3 mg/dl
MCV	50.38±0.99	49.01±0.83	41-54 fl	Tp	6.85±0.49	7.13±0.20	5.2-8.5 mg/dl
MCHC	32.86±0.87	33.05±0.62	29-36 g/dl	Albumin	3.08±0.22	3.39±0.18	2.4-4.1 mg/dl
Plt	359±83	286±42	100-504×10^3/µL	Glucose	217±71	199±29	70-150 mg/dl
				Urine SpG	1.032±0.004	1.032±0.003	>1.025
				Urine GGT/Cr ratio	0.30±0.046	0.68±0.36	0.03-0.56

WBC: White blood cell, Hct: Hematocrit, Hg: Hemoglobin, RBC: Red blood cell, MCV: Mean Corpuscular Volume, MCHC: Mean Cell Hemoglobin Concentration, Plt: Platelet, PKD^+: Polycystic kidney disease positive, PKD^-: Polycystic kidney disease negative, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase, Tp: Total protein, SpG: Specific Gravity, and Cr: Creatinine. No significant differences were observed in hematological and biochemical factors (P>0.01)

Discussion

Epidemiological and prevalence studies and early detection of PKD in cats is a pivotal approach for elimination of the disease from future generations of cattery bred cats. Therefore, a screening program is highly recommended for early detection of PKD in cats. Ultrasonography and genetic testing are two main methods for screening and/or detection of PKD in human and cat (Chapman, 2007; Domanjko-Petric *et al*., 2008), Ultrasound as a noninvasive and easy technique is the most commonly used imaging modality for screening and diagnosis of PKD in cat (Bonazzi *et al*., 2009; Guerra *et al*., 2018). Also, with the use of new imaging approaches, earlier diagnosis of PKD is possible. As PKD could be detected as early as 7 weeks of age in cats by experienced radiologist and through new imaging approaches (Beck and Lavelle, 2001). In a recent study, sensitivity and specificity of ultrasonography for PKD detection in cats were reported as 96.2% and 91%, respectively (Bonazzi *et al*., 2009). As mentioned before, although renal cysts may be readily identified in kittens as young as 7 weeks of age, their absence does not preclude detection at an older age. In fact, the sensitivity of renal cyst detection by ultrasonography increases with the age, because in affected cats, cysts enlarge progressively with age, and this is an imperative factor in screening and breeding programs. In the present study, the presence of PKD in cats significantly correlated with age (P<0.01). The results showed that the higher the age of the patient, the higher the detection probability of PKD in sonography. For each year increase in age, the detection probability of PKD in sonography was increased about 2.62 times. A recent study on prevalence of PKD in Persian and Persian-related cats in Iran showed the prevalence of PKD among Persian cats and in the total population was 33.80% and 31.30%, respectively. In the respective study there was significant association between PKD prevalence and sex and also between PKD and food type. However, there was no significant difference between PKD and age, hair color, eye color, related clinical signs and other kidney abnormalities in ultrasonographic findings (Tavasolian *et al*., 2018). In human and especially in cats, there may be no signs of renal disease or failure until the cysts are enlarged and causing clinical and paraclinical manifestations. Hypertension that is a common complication in humans is controversial in cats and in some studies is documented as a minor increase in mean arterial pressure (Pedersen *et al*., 2003), however, in some other studies it is not documented (Miller *et al*., 1999). In the present study, the biochemistry, hematology and urine analysis results were not significantly different between affected and nonaffected animals. So, it is another cause for the importance of screening programs in breeding.

The results of this study showed that prevalence of PKD was 36.8% in Persian and Persian-related cats presented to Tehran University Hospital. The presence of PKD in cats significantly correlated with age, as for each year increase in age, the detection probability of PKD in sonography was increased about 2.62 times.

Conflict of interest

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.

References

Barrs, VR; Gunew, M; Foster, SF; Beatty, JA and Malik, R (2001). Prevalence of autosomal dominant polycystic kidney disease in Persian cats and related-breeds in Sydney and Brisbane. Aust. Vet. J., 79: 257-259.

Barthez, PY; Rivier, P and Begon, D (2003). Prevalence of polycystic kidney disease in Persian and Persian related cats in France. J. Feline Med. Surg., 5: 345-347.

Beck, C and Lavelle, RB (2001). Feline polycystic kidney disease in Persian and other cats: a prospective study using ultrasonography. Aust. Vet. J., 79: 181-184.

Bonazzi, M; Volta, A; Gnudi, G; Cozzi, MC; Strillacci,

MG; Polli, M; Longeri, M; Manfredi, S and Bertoni, G (2009). Comparison between ultrasound and genetic testing for the early diagnosis of polycystic kidney disease in Persian and Exotic Shorthair cats. J. Feline Med. Surg., 11: 430-434.

Cannon, MJ; Barr, FJ; Rudorf, H; Bradley, KJ; Gruffydd-Jones, TJ and MacKay, AD (2001). Prevalence of polycystic kidney disease in Persian cats in the United Kingdom. Vet. Rec., 149: 409-411.

Chapman, AB (2007). Autosomal dominant polycystic kidney disease: time for a change? J. Am. Soc. Nephrol., 18: 1399-1407.

Domanjko-Petric, A; Cernec, D and Cotman, M (2008). Polycystic kidney disease: a review and occurrence in Slovenia with comparison between ultrasound and genetic testing. J. Feline Med. Surg., 10: 115-119.

Eaton, KA; Biller, DS; DiBartola, SP; Radin, MJ and Wellman, ML (1997). Autosomal dominant polycystic kidney disease in Persian and Persian-cross cats. Vet. Pathol., 34: 117-126.

Guerra, JM; Freitas, MF; Daniel, AGT; Pellegrino, A; Cardoso, NC; de Castro, I; Onuchic, LF and Cogliati, B (2018). Age-based ultrasonographic criteria for diagnosis of autosomal dominant polycystic kidney disease in Persian cats. J. Feline Med. Surg., 21: 156-164.

Iglesias, CG; Torres, VE; Offord, KP; Holley, KE; Beard, CM and Kurland, LT (1983). Epidemiology of adult polycystic kidney disease, Olmsted County, Minnesota: 1935-1980. Am. J. Kidney Dis., 2: 630-639.

Lyons, LA; Biller, DS; Erdman, CA; Lipinski, MJ; Young, AE; Roe, BA; Qin, B and Grahn, RA (2004). Feline polycystic kidney disease mutation identified in PKD1. J. Am. Soc. Nephrol., 15: 2548-2555.

Miller, RH; Lehmkuhl, LB; Smeak, DD; DiBartola, SP and Radin, J (1999). Effect of enalapril on blood pressure, renal function, and the renin-angiotensin-aldosterone system in cats with autosomal dominant polycystic kidney disease. Am. J. Vet. Res., 60: 1516-1525.

Norman, J (2011). Fibrosis and progression of autosomal dominant polycystic kidney disease (ADPKD). Biochim. Biophys. Acta. 1812: 1327-1336.

Paryan, M; Tavakoli, R; Rad, S; Feizi, N; Kamani, F; Mostafavi, E and Mohammadi-Yeganeh, S (2016). Over-expression of NOTCH1 as a biomarker for invasive breast ductal carcinoma. 3 Biotech. 6: 58.

Pedersen, KM; Pedersen, HD; Haggstrom, J; Koch, J and Ersboll, AK (2003). Increased mean arterial pressure and aldosterone-to-renin ratio in Persian cats with polycystic kidney disease. J. Vet. Intern. Med., 17: 21-27.

Tavasolian, P; Rajabioun, M; Salari Sedigh, H and Azizadeh, M (2018). Survey of polycystic kidney disease and other urinary tract abnormalities using ultrasonography in Persian and Persian related cats in Iran. Et. Res. Forum. 9: 99-103.