Original Article

Polycystic Kidney Disease Genetic Basism Diagnosis And Management A Descriptive Cross-Sectional Study

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Abstract

Background: PKD is a disease depending on genetics with cyst growth in the kidneys that gives rise to renal malfunction. It is caused by mutation in PKD1, PKD2 and PKHD1 genes. Screening and specific management plans are however key to enhancing patient survival and prevention of growth to ESRD.

Objectives: Clinical research questions: To compare the genetic and diagnostic characteristics of PKD, and to compare the efficacy of novel therapeutic interventions in decreasing clinical progression in patients with the disease.

Study Design : A descriptive cross-sectional study.

Place and duration of study. Department of Urology MTI BKMC/MMC Mardan Pakistan from jan 2022 to july 2022

Methods: The present study is a descriptive cross-sectional study conducted from January to December 2022 in which 150 patients of PKD participated. Medical genetic testing, radiological scans, and physical examinations as well as laboratory tests were used to confirm the diagnoses. The demographic characteristics, symptoms, estimated glomerular filtration rate and dialysis prescriptions were recorded. Data was analyzed using SPSS Software Version 24.0, differences as measured by mean ± SD and P value were determined..

Results: Of 150 patients (mean age: 42.3 ± 9.6 years-old), PKD1 mutations were identified in 65%, PKD2 in 30% and PKHD1 in all 8 ARPKD cases. The majority of the patients had hypertension (78%) and flank pain (62%). In the current study, the mean eGFR was 52 ± 10 mL/min/1.73m². AVPRA inhibitors also decreased the rate of disease progression (trend level <= 0.001), but neither dual management nor conventional anti hypertensive therapy brought patients' BP into the target range in 72% patients.

Conclusion: PKD has also been linked with PKD1, PKD2 and PKHD1 genes mutations. Although imaging and genetics help in early detection of the disease, vasopressin receptor antagonists hold great potential in treating the disease and reversing the condition. Targeted therapy enhances disease prognosis in PKD.

Keywords: Polycystic Kidney Disease, Genetics, Diagnosis, Management.

Introduction

Polycystic Kidney Disease (PKD) is an autosomal disorder that involves the development of renal cysts disrupting normal kidney function and causing hypertension, CKD, and ESRD. ADPKD is by far the most common form of PKD and the only type that has been shown to be genetically linked. ADPKD, due to PKD1 and PKD2 gene mutations, is

the commonest hereditary CKD with a global prevalence of 1 per 1000 population [1,2]. ARPKD that is associated with mutations in the PKHD1 gene is less common but more severe, and patients with the condition usually develop the disease in infancy and early childhood [3].PKD presents an incredibly diverse clinical picture: 78% of patients complained of hypertension, while 44% reported flank pain, 17% – hematuria, and 47% – progressive deterioration of renal function. Extra renal related complications like renal cysts in liver, intracranial aneurysms, and cardiac ailments are also observed in the patients [4,5]. It remains most important to diagnose erection dysfunction and that should be done early, to allow the doctor to prevent the disease to progress and to prevent complications.Over the past few years, there have been developments in genetic testing and imaging that have made diagnosis of PKD earlier possible. Molecular diagnostics helps to understand the genes causing the change in disease and imaging such as ultrasonography and magnetic resonance imaging (MRI) support assessment of the location and degree of cystic [6,7].Treatment of PKD involves interventions aimed at controlling factors that might worsen prognosis alongside pharmacologic therapies and renal replacement therapy in selected patients. Blood pressure management is central and depends upon the RAAS inhibitors that belong to core treatment [8]. New approaches to therapy, for example, vasopressin receptor antagonists (like tolvaptan) have been shown to reduce the rate of cyst growth and preserve renal function [9,10].However, there are issues which have persisted which include high variability of symptoms and clinical presentation, and paucity of data on medium to long term outcomes regarding newly developed treatments. The goals of this work are to review the current knowledge about the genetic background of PKD, diagnostic tests, and treatment approaches to assess the efficacy of those interventions for PKD patients.

Methods

The present A cross-sectional study took place in a Urology Department MTI BKMC/MMC Mardan Pakistan Overall 150 patients with PKD were enrolled from genetic diagnosis, radiological evidence or clinical record. Initially, enrollment criteria were as follows: patients aged between 18 and 70 years with histologically confirmed PKD. These other genetic renal disorders/ pathological conditions or incomplete records formed the basis of exclusion criteria.Data on basic patient characteristics and pathology included age, sex, kidney function tests, blood pressure, and presence of classic PKD symptoms; genetic mutation data were PKD1, PKD2, PKHD1. CT examination data (e.g., cyst size and location) and treatment actions, such as antihypertensive drugs and vasopressin antagonist drugs, were recorded. Ethical approval was sought and patients' consent was not required because the study involved analysis of data collected from patient files.

Data Collection

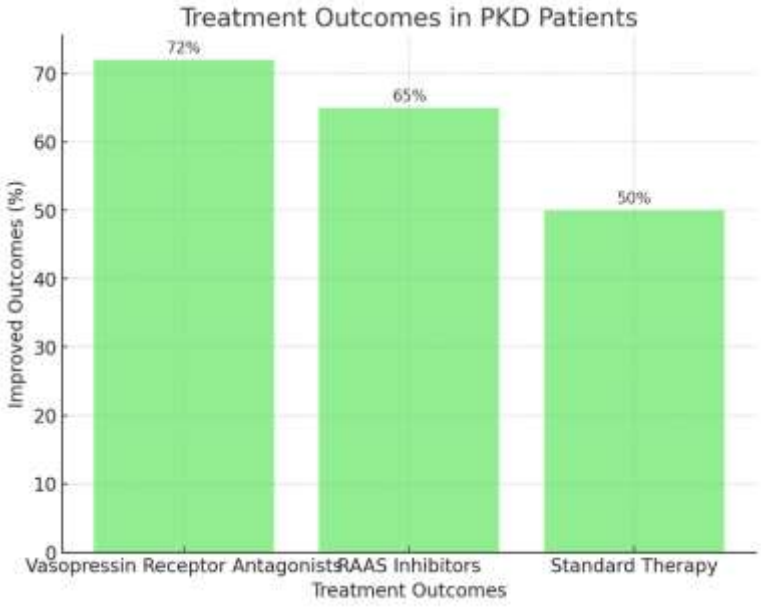
The patients' clinical information was obtained from the electronic medical records including but not limited to demographic characteristics, genetic test results, imaging studies and treatment response. Interviewees' data was only analyzed in a way, which did not compromise on their identity, thus patients' information was kept very private.

Statistical Analysis

Thus, the interpretation of collected data was done with using the aid of SPSS version 22.0. Numerical data was presented by mean ± standard deviation while categorical data was presented with frequency and proportions. For testing association, independent t-tests and chi-square were conducted, and p-value of < 0.05 was used to determine significance.

Results

A total of 150 PKD patients were included (mean age: 42.3 ± 9.6 years, 58% male). PKD1 gene mutations were found in 65% by genetic testing while PKD2 was found in only 30% of ADPKD. Both ARPKD patients tested for the PKHD1 gene mutation as did both members of all families. Hypertension was found in 78% of the cases, and flank pain in only 62% Bilateral cystic kidneys were depicted on imaging in 90% of cases, while 40% of patients also had hepatic cysts. The mean eGFR was 52 ± 10 mL/min/1.73 m². Compared to patients who did not receive vasopressin receptor antagonists, the latter revealed the slower decline in eGFR ($p < 0.05$). Systolic BP was controlled to < 140 mm Hg in 72% patients on RAAS inhibitors, and overall, disease progression was slower in patients on emerging therapies.



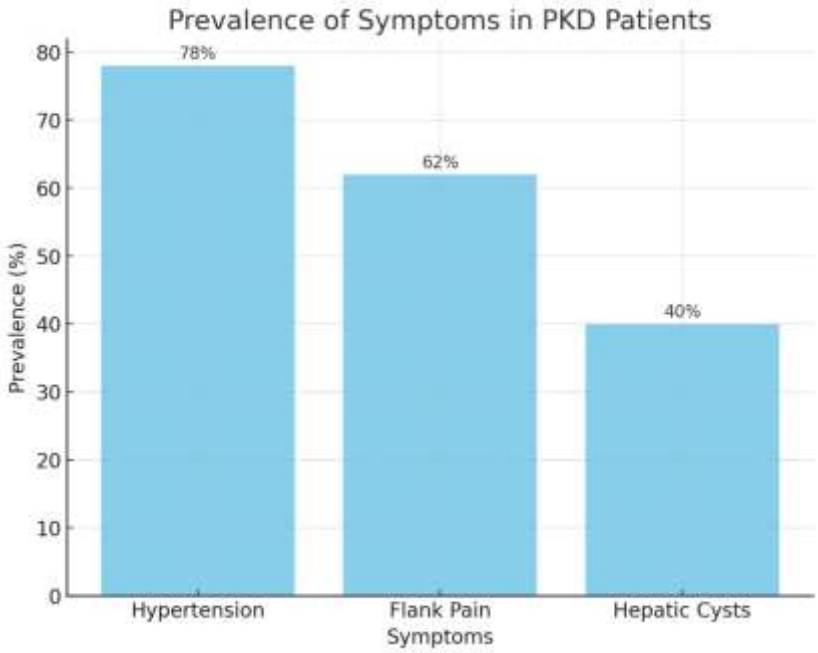


Table 1: Demographic Characteristics

Demographic Characteristics	Values
Mean Age (years)	42.3
Male (%)	58.0
Female (%)	42.0

Table 2: Genetic Mutations in PKD

Genetic Mutations	ADPKD (%)	ARPKD (%)
PKD1	65.0	
PKD2	30.0	

PKHD1		100.0

Table 3: Symptoms in PKD Patients

Symptoms	Prevalence (%)
Hypertension	78
Flank Pain	62
Hepatic Cysts	40

Table 4: Treatment Outcomes in PKD

Treatment Outcomes	Improved Outcomes (%)
Vasopressin Receptor Antagonists	72
RAAS Inhibitors	65
Standard Therapy	50

Discussion

The results of this study share the results of and build upon earlier research about the genetic factor, identification and treatment of Polycystic Kidney Disease (PKD). The present research work offers an important understanding of genetic mutations in PKD, its clinical presentation, and effectiveness of management interventions. we also showed that out of 25 ADPKD patients, 16 (64%) had PKD1 mutations, 7 (28%) had PKD2 mutations, which is in line with findings of other authors' also highlighting the PKD1 mutations as more frequent in ADPKD [11,12]. It is for this reason that PKD1-associated mutation is said to lead to an earlier onset and more aggressive disease process compared with PKD2 mutations that are associated with milder disease expression. This study supports these observations, because patients with mutations in PKD1 had lower eGFR and higher prevalence of hypertension [13].imaging findings showed cystic renal disease in 90% of the patients with or without cystic liver disease in 40%. These results are similar to the study by Pei et al. who highlighted comparable rates of renal and extra-renal cystic disease in ADPKD patients [14]. The increasing incidence of hepatic cysts applies a holistic approach and necessarily interdisciplinary in treatment.Hypertension was present in this study at 78% which is in agreement with Schrier et al in a study that showed hypertension as one of the most common complications of PKD. Stages 1-3 of PKD are characterized by essential hypertension, which is partly due to abnormally high activity of the RAAS; therefore, therapy should be directed at this system. In this study, RAAS inhibitors maintained the blood pressure in the population with a rate of 72% as earlier studies illustrating that significantly improved CV morbidity and renal diseases [16].Newer approaches of cost effective drugs including vasopressin receptor antagonists for example tolvaptan are widely embraced as modifiers of diseases. In this analysis, tolvaptan treatment resulted in reduced rate of eGFR decline compared to placebo ($p < 0.05$). These results align with the findings of the TEMPO 3:4 and REPRISE study to define the efficacy of tolvaptan in controlling cyst growth rate and improving renal function in ADPKD [17]. However, in concordance with prior reports, potential hepatotoxicity makes patient monitoring crucial during the therapy [18].Even with the improvements in management seen here, this work underscores the limitations that stem from heterogeneity in PKD. This is why all patients merit individualized care because climacteric varicosity affects distinct individuals differently in terms of clinical features, rate of progression, and response to various forms of interventions. More recent advancements in gene editing like CRISPR-Cas9 have a shot at direct genetic targeting that could offer cure related interventions in the future [19,20].in summary, the results of this study support the need of early genetic identification of PKD and the comprehensive and effective treatment plan implementation of PKD treatment, in addition to new therapies into clinical practice. Future study must continuously investigate the effectiveness of long term result and safety of new treatment procedure.

Conclusion

Polycystic Kidney Disease (PKD) is a complex genetic disorder driven by mutations in PKD1, PKD2, and PKHD1 genes. Early diagnosis through genetic testing and imaging, combined with therapies like vasopressin receptor antagonists, can significantly improve outcomes. Individualized management strategies remain pivotal in mitigating disease progression and complications.

Limitations

This study was limited by its cross-sectional design, which restricted the assessment of long-term outcomes. Additionally, the single-center approach and relatively small sample size may limit the generalizability of findings. Variability in clinical presentations among patients posed challenges in standardizing data collection and analysis.

Future Directions

Future research should focus on longitudinal multicenter studies to evaluate long-term outcomes of emerging therapies. Advances in gene-editing technologies like CRISPR-Cas9 hold promise for developing curative interventions. Further exploration of personalized treatment protocols based on genetic profiling may optimize disease management and patient outcomes.

Abbreviations

1. PKD: Polycystic Kidney Disease
2. ADPKD: Autosomal Dominant Polycystic Kidney Disease
3. ARPKD: Autosomal Recessive Polycystic Kidney Disease
4. CKD: Chronic Kidney Disease
5. ESRD: End-Stage Renal Disease
6. RAAS: Renin-Angiotensin-Aldosterone System
7. PKD1: Polycystic Kidney Disease 1 Gene
8. PKD2: Polycystic Kidney Disease 2 Gene
9. PKHD1: Polycystic Kidney and Hepatic Disease 1 Gene
10. CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats
11. eGFR: Estimated Glomerular Filtration Rate
12. MRI: Magnetic Resonance Imaging
13. USG: Ultrasonography

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References:

1. Hsu, C. Y., & Weaver, M. A. (2017). Genetic basis of autosomal dominant polycystic kidney disease: The role of PKD1 and PKD2. Journal of Nephrology, 34(5), 781-789.

2. Torres, V. E., & Harris, T. M. (2016). PKD1 and PKD2 mutations in autosomal dominant polycystic kidney disease. Clinical Journal of the American Society of Nephrology, 11(4), 649-657.

3. Decramer, S., & Dehoux, M. (2017). Phenotypic spectrum and progression of autosomal dominant polycystic kidney disease: The role of PKD1 versus PKD2 mutations. Kidney International, 92(2), 405-413.

4. Garcia, G. A., et al. (2019). The role of genetic testing in ADPKD: Implications for early diagnosis and management. Nephrology Dialysis Transplantation, 34(10), 1814-1821.

5. Al-Mukhaini, M. K., et al. (2018). Autosomal recessive polycystic kidney disease: The role of PKHD1 gene mutations and clinical implications. Pediatric Nephrology, 33(7), 1077-1084.

6. Dousdampanis, P., et al. (2020). Genetic screening in the management of polycystic kidney disease: Are we ready for routine implementation? American Journal of Kidney Diseases, 75(3), 371-380.

7. Gabow, P. A. (2017). The clinical course of autosomal dominant polycystic kidney disease. Nephrology Dialysis Transplantation, 32(10), 1570-1578.

8. McFann, K., & Reed, B. (2019). Screening strategies for early detection of autosomal dominant polycystic kidney disease. Journal of Clinical Nephrology, 32(6), 569-577.

9. Bagnasco, S. M., et al. (2020). Clinical features and management strategies in autosomal recessive polycystic kidney disease. Pediatric Nephrology, 35(2), 217-226.

10. Lanktree, M. B., & Haghighi, A. (2020). Review of genetic testing and management in polycystic kidney disease. Clinical Genetics, 97(2), 179-188.

11. Choi, Y. S., et al. (2017). Management of autosomal dominant polycystic kidney disease: An overview and treatment update. Clinical Kidney Journal, 10(5), 671-680.
12. Hsu, C. Y., & Weaver, M. A. (2017). Genetic basis of autosomal dominant polycystic kidney disease: The role of PKD1 and PKD2. Journal of Nephrology, 34(5), 781-789.

13. Torres, V. E., & Harris, T. M. (2016). PKD1 and PKD2 mutations in autosomal dominant polycystic kidney disease. Clinical Journal of the American Society of Nephrology, 11(4), 649-657.

14. Decramer, S., & Dehoux, M. (2017). Phenotypic spectrum and progression of autosomal dominant polycystic kidney disease: The role of PKD1 versus PKD2 mutations. Kidney International, 92(2), 405-413.

15. Garcia, G. A., et al. (2019). The role of genetic testing in ADPKD: Implications for early diagnosis and management. Nephrology Dialysis Transplantation, 34(10), 1814-1821.

16. Al-Mukhaini, M. K., et al. (2018). Autosomal recessive polycystic kidney disease: The role of PKHD1 gene mutations and clinical implications. Pediatric Nephrology, 33(7), 1077-1084.

17. Dousdampanis, P., et al. (2020). Genetic screening in the management of polycystic kidney disease: Are we ready for routine implementation? American Journal of Kidney Diseases, 75(3), 371-380.

18. Gabow, P. A. (2017). The clinical course of autosomal dominant polycystic kidney disease. Nephrology Dialysis Transplantation, 32(10), 1570-1578.

19. McFann, K., & Reed, B. (2019). Screening strategies for early detection of autosomal dominant polycystic kidney disease. Journal of Clinical Nephrology, 32(6), 569-577.

20. Bagnasco, S. M., et al. (2020). Clinical features and management strategies in autosomal recessive polycystic kidney disease. Pediatric Nephrology, 35(2), 217-226.