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Prevalence, risk factors and disease knowledge of polycystic kidney disease in Pakistan

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Abstract

Polycystic kidneys disease refers to cyst(s) formation in kidneys with severe consequences of end stage renal disease thus have higher mortality. It is a common genetic disease occurring either as autosomal dominant polycystic kidney (ADPKD) or autosomal recessive polycystic kidney disease (ARPKD) with prevalence rates of 1/1000 and 1/40,000 respectively. Dominant forms presenting in later (>30) while recessive in earlier ages (infancy) and affecting both sexes and almost all race. The patient experiences many renal as well as extra-renal manifestations with marked hypertension and cyst formation in other organs predominantly in liver. Due to genetic basis, positive family history is considered as major risk factor. Ultrasonography remains the main stay of diagnosis along with family history, by indicating increased renal size and architectural modifications. Initially disease remains asymptomatic, later on symptomatic treatment is suggested with surgical interventions like cyst decortications or drainage. Dialysis proved to be beneficial in end stage renal disease. However renal transplantation is the treatment of choice.

Keywords

disease knowledge, Pakistan, polycystic kidney, prevalence, risk factors

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Introduction

Polycystic kidney disease is a condition characterized by formation of multiple cysts in one or both kidneys and progression in size and number of cysts leads to renal enlargement and insufficiency along with extra renal manifestations. Cyst is a fluid filled space lined by epithelial cell and supported by connective tissue.[1] In case of cystic kidney it is an out pouching that can arise from any part of nephron, collecting ducts or glomerulus.[2] The number and the size of cysts increases with age. Cystic kidney expansion is greater in man than in women.[3] PKD is classified in two types referred to as PKD-1 and PKD-2 depending on genetic basis and clinical presentation. A study indicated that genetic abnormality governs the cystic initiation not the enlargement, on the basis of observations that the size and number of cysts was greater in polycystic kidney disease-1 (PKD1or Type I disease) than polycystic kidney disease-2—(PKD2 or Type II disease) at base line and the absolute change in PKD 1 kidney size was also greater than that of PKD 2, but the growth rate among both types (5.68% vs 4.82% yearly) was not significantly different.[3] The severity of disease increases when inherited from mother rather than from father.[4] Polycystic kidney disease (PKD) appears in later age, approximately 10%

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Table 1. Risk factors.

Risk factors for ESRD due to polycystic kidney disease
Positive family history
Long term dialysis
Drugs that is, excessive analgesic drugs and exposure to heavy metals, acetaminophen[1]
Age (>30 for ADPKD and <30 for ARPKD)
Male gender
African Americans and patient of sickle cell anemia
PKDI gene
Cardiovascular conditions; Hypertension, increased left ventricular mass
In women; hepatic cysts, three or more pregnancies
Renal conditions; gross hematuria, urinary tract infections in men, renal volume

people have identified cystic kidney at age of 50 to 70.[2] Polycystic kidney disease has high impact regarding morbidity, hospitalization, mortality, and cost to society. PKD is one of the life threatening diseases of kidney. It is common genetic kidney disease leading to End stage renal disease ESRD indicating dialysis and even renal transplantation as ultimate treatment.[5] Although the disease occurs mostly due to genetic causes but there are also acquired causes of cyst formation in kidneys. The most common risk factors of PKD is positive family history. Family history is a cheap and easy way to approach the diagnosis of ADPKD. Taylor et al.[6] conducted a large cohort of 637 subjects with ADPKD for family history analysis as a tool for diagnosis, which led to the initial ADPKD diagnosis in 49% of all subjects overall and study revealed that advances in knowledge of and potential interventions for ADPKD have led to increased use of family history screening. Other factors may include aging in case of simple cysts; whereas drugs and hormones may also considered and in multiple cysts of kidney, long term dialysis is considered as risk factors for progression to ESRD (Table 1).[7,8]

Prevalence of polycystic kidney disease in Pakistan

The prevalence of PKD in Pakistan is comparable to figures of USA where it is responsible for 4.2%2 while in ARPKD 0.6% of patients before age of 20 years in USA[3] and 1.5% in Europe[4] of ESRD in children. Every year 2144 people bear renal replacement therapy in USA.[5] The ADPKD is found in whole world affecting over 15 million people among all races but most commonly is responsible for 5% to 10% of ESRD in white people as compared to black African Americans.[6] The prevalence of ADPKD in Copenhagen is one per 1000.[7] The prevalence is low in France that is, one per 1111,[8] in Japan it is estimated as one per 4033[9] and in Wales one per 2459.[10] The prevalence varies among races in Seychelles, black population found to be rarely affected while whites have one per 544. In Olmsted Country, USA and MN the prevalence lies between one per 400 and one per 1000 in observed, autopsy cases and clinically diagnosed patients respectively.[11,12] The prevalence of diagnosed ADPKD is 1:4033 in general population of Japan it is almost one tenth of the autopsy based prevalence.[13] The prognosis is better in patients having age greater than 70 years compared to those <70 years. In the earlier studies in Japanese population the prognosis seems to be improved, assumed to be due to facilities of early diagnosis, improved clinical management, improved environmental factors, and diagnosis with mild phenotype.[9] As the kidney diseases are ascending in South Asian Countries including Pakistan, the main stay behind is the lack of awareness in population and increasing risk factors along with insufficient and cost effective health care facilities. It is estimated that the annual incidence of new cases of end-stage renal disease (ESRD) in 1 year is 150 to 200 per million population in Pakistan. Due to paucity and non registry of cases the exact data in Pakistan is not known yet the estimated percentage of ADPKD patients out of these ESRD cases/ year is 2% to 3%.[14]

Pathogenesis of PKD

The PKD can be inherited as autosomal dominant trait or autosomal recessive trait. The genes responsible for pathogenesis of PKD are PKD1 and PKD2

Table 2. Proteins and their responsible genes.

	Genes			Proteins				
	Genes	Size (kb)	No of exons	Proteins	Localization	Calculated mass (kDa) of protein	Size of protein(aa)	Proposed function
ADPKD	PKD 1	~50	46	Polycystin1	Primary cilium, Tight junctions, adherent junctions, desmosomes, focal adhesions	460	4302	Cell to cell & cell to matrix interactions, signaling and ion transport.
	PKD 2	~68	15	Polycystin2	Primary cilium, centrosome, endoplasmic reticulum.	110	968	Ion transport
ARPKD	PKHD 1	~469	86	Fibrocystin	Primary cilium	447	4078	Promotes growth and proliferation of renal cells.
					Apical membrane			Act as receptor and interact with extracellular molecules

along with PKHD genes. The mutations in genes PKD1 (85%–90% cases) and PKD2 (10%–15% cases) are mostly associated with ADPKD[10] where as PKHD mutation is associated with ARPKD. PKD1 is located on short arm of chromosome number 16 (16p13.3 region)[11] while PKD2 is present on long arm of chromosome number 4 (4q21.2 region).[1,12] The proteins encoded by the responsible genes PKD1 and PKD2 are polycystin 1 and polycystin 2, respectively.[13]

Genetically unresolved cases of ADPKD directed further research studies which indicated that sequencing of six genetically unresolved ADPKD-suffering families identified a strong candidate GANAB gene with a missense mutation, encoding glucosidase II subunit α (GII α). By analyzing GANAB-null cells an absolute requirement of GII α for maturation and localization of ADPKD proteins that is, polycystin 1 and polycystin 2 on surface and ciliary structures, and reduced mature polycystin 1 was seen in GANAB mutant cells. Overall, it is shown that GANAB mutations cause ADPKD and that the cystogenesis is most likely driven by defects in PC1 maturation (Table 2).[14]

The structures of these encoded proteins have been predicted with the assistance of gene mapping and molecular applications and even the DNA sequencing has also been done of PKD1 and PKD2.[10,15] These are membrane proteins[16,17]; located mostly on hair like surface structures[16–18] termed as primary cilium[16,19]; anchored with the help of basal body in to the cell body of most mammalian cells.[17,18,20] The cilium found on cells of nephrons and is acting as apical projections of renal epithelium in to the tubular lumen and thus polycystins found on them serve as sensor to the response created by flow of ions from the lumen. In the cells bearing PKD1 no change in appearance of cilia is seen, rather the ability of cell to detect the change in flow is diminished.[15,16] The pathogenesis of PKD based on the defective proteins due to mutant genes and in turn abnormal structural formation of cilia.[17] It do so by interrupting any of primary cilium regulates many signaling path ways such as Hedgehog, Wnt/b catenin, planar cell polarity (PCP), cyclic adenosine monophosphate (cAMP), and intracellular Ca^{2+}.[18–20] Polycystin 1 contain some functional domain, similar to other proteins found on basal body and primary cilia and are responsible for other cystic conditions of kidney. But it has some transmembrane regions with which it attaches to membrane and form large extracellular area to interact with surface molecules of other cells or substances found in extracellular matrix and also interact with polycystin 2 in adjacent endoplasmic reticulum.[21] According to normal physiological conditions, the interacting polycystin 1 and 2 design a "receptor-ion channel complex" in which polycystin 1 is responsible for sensation of luminal sheer stress and opens polycystin 2, which is a non-selective calcium channel Ca^{2+}.[22,23] Polycystin 2 physically interacts with a store operated Ca^{2+} transient receptor potential channel 1 (TRPC 1).[24] It is proposed that the

primary cilia become curved due to flow of fluid through renal epithelium and induce intracellular Ca^{2+} influx. The changes in intraluminal pressure also induce the arterial response, which is affected by polycystin 1 to polycystin 2 ratio in the arterial myocytes by regulating "stress activated cation channels" thus plays a key role in maintenance of intracellular Ca^{2+} homeostasis in vascular smooth muscles. PCP controls polarized cell division, direction of cell migration and cellular differentiation to assist in organogenesis of organ systems.[18] The disruption of any or all of these signaling cascades produce dedifferentiation of cystic epithelium, abnormalities of basement membrane, uncontrolled division of cells, impaired secretory characteristics of epithelia and or altered polarized state of cell.[25,26] Ultimately the cystic expansion compresses the normal renal tissues causing apoptosis and intrarenal ischemia due to compression of renal vessels leading to stimulation of renin angiotnsin aldosteron system that in turn is responsible to increased vascular resistance, sodium retention, progressive cystic enlargement and finally renal fibrosis.[27] In vitro studies suggest the proliferation of epithelial cells of ADPKD patient supporting the idea that formation of normal renal tubular structures are controlled by apoptosis after birth, but it becomes persistent and proliferation continued.[28,29] Another theory suggested that fluid enters in the cyst instead of leaving it, because of basolaterally oriented Na^+/K^+ ATPase, abnormally located at apical position.[30] Shifting of another channel that is, Na/K/2Cl symporters to epithelial cells basal surface is other contributing factor to pathogenesis of polycystic kidney disease.[31]

Disease course of polycystic kidney

The disease course of patient having PKD2 defects presents less severity with slower and later onset of symptoms and slow progression to renal failure thus show longer life expectancy of about 69.1 years, whereas PKD1 defect is more severe with shorter life expectancy of 53.0 years and early onset of symptoms leading to rapid progression to renal failure approximately 16 years earlier than former[32] and high risk of ruptured intracranial aneurysm where 8% to 11% ADPKD patients die due to ruptured intracranial aneurysm.[33] Intracranial aneurysms is a vascular manifestations in ADPKD and occurs infrequently (5%–9%), but 3- to 5-fold more frequent than in general population. Proper detection of risk factors for intracranial aneurysm formation in ADPKD is crucial and can allow for targeted patient screening and risk factor reduction. These data are critical given the significant morbidity and mortality (between 40% and 60%) associated with intracranial aneurysm rupture in ADPKD.[34] The single gene mutation encounters less severe disease course and not much worse outcomes compared to mutations on both PKD1 and PKD2 that is not much common.[3] Although there are some cases of polycystic kidney disease having neither PKD1 nor PKD2 defects, and predicts the presence of PKD3 gene involved in the pathogenesis of condition, but PKD3 is not yet identified.[35,36]

Autosomal dominant polycystic kidney disease (ADPKD): occurring in approximately one in every 1000 people, with fewer than 300,000 diagnosed in the United States.

Autosomal dominant polycystic kidney disease (ADPKD) affects 4 to 6 million people worldwide.[37] The disease is more prevalent in men than in women. The dominant form means that 50% of children of affected parents will inherit the disease. ADPKD not only affects the adults as it is known as "adult polycystic kidney disease," but new born and young children also found affected by this type of cystic disease.[37] Patients with ADPKD suffer from many renal as well as extra-renal anomalies (Table 3).

The most common extra-renal complications that contribute to morbidity and mortality in ADPKD patients are of cardiovascular nature. It is believed that distortion of the renal parenchyma leads to structural damage, tubular dysfunction, and renal vascular ischemia and results in activation of the RAAS furthermore GFR decline occurs after extensive vascular remodeling and an altered intimamedia thickness of carotid arteries, impaired endothelial-dependent vascular relaxation, and vascular ultrasound thickness in ADPKD patients. As Cilia are a local regulator of blood vessel, ciliopathy plays a key role in CVD development.[38] Moreover studies demonstrates a high prevalence of cardiovascular risk factors including hypertension, obesity, diabetes and hypercholesterolemia in ADPKD population. Cardiac diseases are most common cause of death (34%) in ADPKD patients with end stage renal disease (ESRD) and next to cardiac diseases are infections that cause approximately 20.4% of deaths in such patients.[39] Although

Table 3. Renal and extra-renal manifestations of ADPKD.

Renal manifestations	Extra-renal manifestations
Renal cyst	Cyst formation in; liver, pancreas, lungs, spleen, seminal vesicles, arachnoids membrane.
Adrenal adenoma	Abdominal wall hernias
Renal calculi	Colonic diverticula
Urinary tract infections	Cardiovascular; aneurysm of aortic root and iliac and cerebral artery, dolichoectasias, megadolichobasilar artery, mitral valve prolapse
Renal insufficiency	

various patients with ADPKD never reach end stage renal disease and others may suffer from ESRD in advanced age,[40] 57% and 50% of ADPKD patients are reported to be surviving with no end stage renal disease at 58 years of age by Churchill et al. and Parfrey et al.[41] respectively. There are certain factors that are found to have association with ADPKD while other much related factors have no association with disease. The factors in Table 1 are associated with severe renal function deterioration in ADPKD and the disease is not found to be associated with affected parent's gender, intracranial aneurysms, women with UTI or men with hepatic cyst, pregnancy[42] and mitral valve prolapse.[40]

Clinical manifestations

The dominant type of disease remains dormant initially and becomes clinically presented at age of 30 to 50 years.[6,43,44] The symptoms include excessive enlargement of both kidneys due to multiple cysts, discomfort in lower abdomen or loin, renal colic or acute loin pain or pain in flanks, hypertension is considered the most prominent clinical feature of disease and found in 80% of cases.[13] The underlying mechanism of hypertension is expected to be the secretion of renin due to stretching of renal tubules bearing cysts. Hematuria, the other symptom, appears first at about 30 years of age in about 19% to 35% of patients as a result of cystic hemorrhage.[13,45] Patient may also show the symptoms like urinary tract infection, cyst infection, polyurea, lower back pain, dyspnea, early satiety,[18,46] renal stones. Kidney stones are found in 20% to 30% of patients[47] that are typically composed of uric acid or calcium, the concentrating defects caused by impaired medullary trapping of ammonia and its conversion to urine leads to reduced excretion of ammonia and low citrate concentration and low pH of urine are considered as contributory factors for stone formation.[6] The pain characterized as severe, debilitating in back, abdomen, or flank remains parallel to hypertension, in incidence of about 60%.[48] Until 30 to 40 years of age, the glomerular filtration rate (GFR) remains normal but the rate deteriorates rapidly after this age[49,50] and patient becomes suggestive to transplantation or most commonly dialysis at age of 70 in 50% of cases.[51] The ultimate consequence of polycystic kidney disease is end stage renal disease that is developed by 45% of ADPKD patients at 60 years of age.[40] The occurrence of renal cell carcinoma/adenoma is 1 in 4 or 5 ADPKD patients and is rare as compared to generalized population and if happened it usually appears multicenteric (28% vs 6%), bilateral (12% vs 1%–5%) and sarcomatous (33% vs 1%–5%).[52] Ultrasound reveals solid mass, CT or MRI guided speckled calcification, tumor thrombus, contrast enhancement and regional lymphadenopathy findings show suspiciousness to carcinoma.

Autosomal recessive polycystic disease

Autosomal recessive polycystic disease (ARPKD) is a common inherited disease characterized by development of cysts in kidneys of fetuses or young children and responsible for high infant mortality[53] usually due to respiratory complaints rather than renal malfunctioning. Occurrence of disease in new born is 1/6000 to 1/55,000.[24,54] The recessive form means that 25% children of two carrier parents will be affected by cystic kidneys. In recessive form the dilatation usually remains limited to collecting tubules of the nephrons and this is because of typical development of cysts here. The disease is rare comparative to ADPKD and is always bilateral with severe outcomes due to manifestation in early ages of infancy, early or late child hood, but disease also manifests in early adult hood in rare cases. On the basis of age of occurrence, number of collecting ducts dilatation and extent of hepatic fibrosis[55] ARPKD is classified as

Table 4. Forms their presentations and outcomes of ARPKD.

Forms of ARPKD	Presentation	Outcome
Perinatal	Pulmonary hypoplasia	Few days' survival, complicated pregnancy.
Neonatal	Mild hepatic fibrosis, cystic distortion of 90% of nephrons, renal malfunctioning.	ESRF
Infantile	Cystic involvement of only few nephrons, portal hypertension, hyperspleenism	Survival up to few years, ESRF
Juvenile	<10% nephrons involved in cystic distortion, little or no renal malfunctioning, portal hypertension, hepatic fibrosis.	ESRF

perinatal, neonatal, infantile and juvenile, all are related to single gene mutation (Table 4).

Mutations on PKHD 1 gene that is found on chromosome number 6p21 are responsible ARPKD. The gene encodes a protein called Fibrocystin/polyductins. Fibrocystin found excessively in infant's collecting tubules and serve as a membrane receptor to interact extra-cellular as well as intracellularly with proteins and sites of phosphorylation, respectively.[56] The pathogenesis of ARPKD is similar to ADPKD. The anatomical changes in renal architecture include bilaterally distended kidneys with sonographically identified multiple small cysts and medullary to cortical parenchyma contain cylindrical spaces arranged along the radius. Extra-renal manifestations of ARPKD is congenital hepatic fibrosis (portal and interlobular) as most prominent feature along with small branches of distal portal vein and hyperplasia of biliary duct and caroli's disease,[6] abnormal extremities, pulmonary hypoplasia, spinal deformities an face appears odd.[57] The disturbance in PCP pathway is totally responsible for ARPKD because mutation on PKHD1 gene causes loss of cell oriented division which, unlike PKD1 and PKD 2, appears as an etiology of cyst formation rather than as a consequence.[25] Although extra renal cystic involvement is less common in recessive type than in dominant form yet liver is considered as most susceptible to abnormalities in ARPKD with hepatomegaly and fibrosis, cholangitis, portal hypertension other presentations are similar to ADPKD. The presentation of a pregnant woman, usually in third trimester, with severe oligohydramnios, placentomegaly but normal renal architecture and fetal sonography reveal bilateral, enlarged, smooth and hyperechogenic kidneys, small or absent urinary bladder are suggestive of ARPKD, with termination of pregnancy as ultimate outcome.[58]

Presence of cystic kidney/kidneys in any other relative of patient or even three generations previous ancestors is suggestive of polycystic kidney disease. The diagnosis of ADPKD depends largely upon the positive family history of patient, with negative family history of ADPKD the presence of bilateral renal enlargement or presence of extra renal cysts can also be helpful in making the diagnosis of ADPKD.[59] The diagnosis of PKD is primarily based on imaging criteria in an individual with positive family history. The number of cysts in kidney and involvement of one or both kidneys also provides a way to the diagnosis and this can be achieved by using sonographic techniques. These techniques has advantages of early detection of complications so as to manage before further damage and also for other aspects of life for example, family planning, selection of donor for kidney transplantation having no risk of cystic development, on the other hand it implicates certain psychological stress leads to educational, professional or social disturbance. Ultrasound remains the main stay of diagnosis as it is cost effective and safe. The clinical criteria for ARPKD is based upon identified hepatic fibrosis in patient and on the other hand no evidence of renal cyst in both parents, obvious structural distortion of kidney in affected sibling on ultrasound.[60] Ultrasonographically found two cysts in one or both kidneys at an age of about 30 years or less, two cysts in both kidneys at 31 to 59 years or four cysts in both kidneys at or over the age of 60 years makes strong diagnosis of ADPKD.[61] The above criteria are 100% sensitive for people of 30 years or older and for patients having PKD 1 mutations, while in PKD 2 mutations in patients younger than 30 years have 67% sensitivity.[62] In ARPKD antenatal ultrasound is diagnostic only in severe cases. CT scan and MRI are highly sensitive but costly. These techniques provide anatomic description and extent of cystic expansion and are considered in case of complicated cysts. To identify the genetic basis of disease, genetic testing is performed. Genetic testing isn't ordinarily used to make a finding of ADPKD if physicians are as of

now sure you have ADPKD. On the off chance that somebody in your family has ADPKD and you or others are being verified whether you may have it as well, at that point an abdominal ultrasound might be utilized. This is on the grounds that cysts in the kidney can frequently be identified at a beginning phase by a ultrasound. Genetic testing to affirm whether you have a defective PKD gene may be useful in these circumstances:

- to affirm whether you have ADPKD on the off chance that you have no side effects yet or physicians are questionable of your conclusion
- if you are thinking about giving a kidney to a relative with ADPKD

on the off chance that you are thinking about having kids, to assist you with deciding. It can be done by two methods that is, sequence or linkage analysis and the later is chosen by less than 50% of candidates due to requirement of involving multiple family members. Highly informative micro satellite markers flanking PKD1 and PKD2 are used in linkage analysis. Molecular testing by direct analysis is difficult to perform because of complex and large sized PKD1 and its related alleles. Denaturing high performance liquid chromatography (DHPLC) is used for mutation scanning with detection rates of 65% to 70% for PKD1 and PKD2 mutations[63,64] and now it becomes 85% by direct sequencing.[65] Blood tests are also performed to check the variations in plasma concentrations of certain agents as serum creatinine and reduced concentration of Na (hypernatremia) is diagnostic for ARPKD. Plasma levels of vasopressin are increased (due to destruction of medullary architecture). Blood and urine culture are done to confirm the presence of infection and type of organism.

The disease remains asymptomatic in early stages and treatment is not suggested until certain indications appeared (Table 5).

Table 5. Treatment indications for PKD.

Indication for treatment of PKD
Uncontrollable HTN
Severe back/loin pain
Abdominal fullness
Progressive cystic enlargement
Hematuria/hemorrhage
Recurrent infection

The pain is most troubling feature of polycystic kidneys caused due to multiple reasons like increased mass induced stretching, abscess formation or hemorrhage in cyst or calculi formation tumor and leading obstruction. It is important to relieve the pain and is done by use of analgesics, but most commonly used analgesics are NSAIDs has complications of further deterioration of kidney functioning due to renal clearance of these agents, modification of life style, reassurance use of tricyclic antidepressants and to avoid aggravating factors are important steps to be taken. For acute pain management narcotic analgesics can be recommended and the blockage of splenchnic nerve by local anesthesia might be helpful.[66,67] If analgesics are not proven to be beneficial then nephrectomy is the treatment of choice for pain management in patients with end stage renal diseases. Other surgical interventions may include aspiration of cyst followed by use of sclerosing agents to prevent fluid reaccumulation. In case of multiple cysts laproscopic or surgical fenestration of cyst via lumber or flank incision,[68] while in case of small cysts renal denervation through laparoscopy or thoracoscopy can be performed.[69,70] The antihypertensive drugs having least side effects and marked reno-protection are ACE inhibitors or angiotensin receptor blockers that induce increase in renal blood flow,[71,72] reduction in proteinuria and left ventricular hypertrophy thus improve renal functions.[73–75] Renal calculi are conservatively treated by hydration therapy and alkalinization but radiation therapy has good results without serious complications variable methods are available that is, extracorporeal shockwave lithotripsy and percutaneous nephrostolithotomy. Hemorrhage is treated by bed rest, analgesics and hydration therapy but in case of excessive bleeding or hematoma formation, segmental artery embolization is indicated. In case of ARPKD intensive care and prolonged ventilation is required to cope with respiratory complications. The medical treatment aim at improving the basic factors that lie behind the pathology of polycystic kidney disease, the most important is cellular proliferation. The role of chemotherapeutic agents, like tyrosine kinase inhibitors,76 Erb-B1 inhibitors (Epidermal growth factor receptor),[76] Src kinase,[77] MEK,[78] CDK,[79] Sirolimus,[80] and paclitaxel,[81] in management of PKD has supported by many

experiments on animal models and experienced to have efficacy in human patients of PKD also. A recent review of literature supports the performance of open or laparoscopic cyst decortications procedures for control of pain and infection without the worry of causing further renal impairment in those with preserved renal function. Lipophilic antibiotics will be beneficial in case of infected cysts because others are not able to penetrate in cysts. Surgical treatment options include open cyst decortications and laparoscopic decortications with robotic surgery that is very effective in ADPKD patients for pain management by removing superficial as well as parenchymal cysts, performed in simple and radical nephrectomy and pyeloplasty like retroperitoneal procedures. End stage renal disease the most serious and life threatening outcome of polycystic kidney disease responds well to dialysis due to high levels of hemoglobin and erythropoietin or low comorbidity.[82] In case of kidneys not excessively enlarged peritoneal dialysis is suitable while renal transplantation remains the treatment of choice in end stage renal disease with similar results as of causes other than polycystic kidneys. Renal transplantation is followed by certain complications that is, diabetes mellitus and cardiovascular diseases.[83] For the hepatic cysts no treatment is recommended until it become symptomatic, the interventions such as percutaneous cyst aspiration, laparoscopic hepatic cyst fenestration, combined liver resection and cyst fenestration, liver transplantation are available options to reduce size of cyst as well as liver.[84,85] For intracranial aneurysm less than 7 mm in size and detected on presymptomatic screening, conservative treatment is recommended. Avoiding smoking, controlling of blood pressure and hyperlipidemia show beneficial results in patients of intracranial aneurysm. The water intake is itself the most convenient factor to improve renal abnormalities especially PKD due to vasopressin suppression.[86]

Prospects for the future

The recognition of associated as well as non-associated factors of disease is very important because they have crucial effects on progression of disease. It will also become helpful to reduce the progression of condition to end stage renal disease by applying appropriate interventions.

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The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical statement

Our study did not require an ethical board approval because it did not contain human or animal trials.

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