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Review

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Empowering women at the heart of autosomal dominant polycystic kidney disease: Addressing unique challenges gender-sensitive approach

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Abstract

Autosomal dominant polycystic kidney disease is a genetic disorder characterized by the progressive development of renal cysts, leading to end-stage renal disease in a significant proportion of affected individuals. While the disease affects both men and women, emerging evidence suggests that sex differences may influence the clinical presentation, progression, and response to treatment in autosomal dominant polycystic kidney disease patients. Based on our experience, women are diagnosed earlier and often experience more symptoms like chronic pain and microhematuria. However, disease progression tends to be slower. Hormonal therapy, controversial due to its impact on cyst growth, is important for contraception and conditions like polycystic ovary syndrome, endometriosis, and menopause. Copper intrauterine devices are the safest contraceptive option, while progestin-only methods are recommended for those who cannot take estrogen. This review aims to explore the implications of gender differences in autosomal dominant polycystic kidney disease, highlighting the need for personalized approaches to diagnosis, monitoring, and management. Emphasizing the integration of gender-based insights into clinical practice could ultimately lead to more tailored therapeutic strategies, improving patient outcomes in autosomal dominant polycystic kidney disease.

Keywords

ADPKD, gender medicine, disease progression, personalized medicine, hormonal factors

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Introduction

Gender medicine

In recent decades, gender medicine has gained increasing importance as a fundamental discipline for understanding the biological and sociocultural differences between sexes and their impact on health. Traditionally, medical research has relied predominantly on uniform models, leading to the generalization of results that often fail to accurately reflect the specific needs and physiological responses of

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individuals.[1] It is now widely recognized that men and women can exhibit different manifestations of the same disease and respond differently to treatments.[2]

This article aims to explore the influence of sex on genetic imprinting, pathogenesis, diagnosis, clinical, therapeutic, and psychological aspects in autosomal dominant polycystic kidney disease (ADPKD). Through an in-depth analysis of differences in symptoms, disease progression, the role of pregnancy, and the perception of the disease between men and women, we aim to highlight the importance of adopting a more inclusive medical approach that is attentive to gender-specific differences.

As one of the leading referral centers in Italy for genetically determined cystic diseases, with a particular focus on ADPKD—a condition that, due to its multifactorial nature, often requires a multidisciplinary approach[3]—we wish to share come reflection based on our clinical experience and the evidence available in the literature.

Starting from our clinical experience, we chose to focus on several key aspects of the issue and undertake a robust analysis of the existing literature, ensuring that our findings were grounded in both practical insight and evidence-based research.

Autosomal dominant polycystic kidney disease

ADPKD is the most common inherited renal disorder, with an estimated prevalence of ~4 in 10,000 individuals according to recent epidemiological studies.[4–6] This genetic condition is characterized by the formation and progressive growth of cysts, which cause an increase in kidney volume and a gradual decline in renal function. ADPKD follows an autosomal dominant inheritance pattern.[4–8] Mutations in the PKD1 gene and the PKD2 gene are the primary causes of ADPKD, encoding for the proteins polycystin-1 and polycystin-2, respectively. Other genes, such as GANAB, DNAJB11, ALG8, and IFT140, may also be involved in a minority of cases.[9–11] Symptoms typically manifest between the third and fourth decades of life, and patients with truncating mutations in the PKD1 gene tend to present with a more severe clinical course.[12]

Common signs include arterial hypertension, hematuria, abdominal pain, nephrolithiasis, development of liver and pancreatic cysts, and the presence of diverticula. Cardiovascular abnormalities are also frequent, including heart valve defects and cerebral aneurysms.[7] The gradual reduction in glomerular filtration rate (GFR), associated with an increase in renal volume, ultimately results in chronic kidney disease (CKD). Monitoring and controlling blood pressure (BP) are essential for mitigating disease progression.[13]

A peculiar aspect of ADPKD is abdominal enlargement, caused by the presence of large cysts and overall organomegaly. Liver cysts, the most common extrarenal manifestation, can cause symptoms such as abdominal pain, bloating, dyspnea, infections, and hemorrhages. Large cysts may lead to significant hepatomegaly, resulting in polycystic liver disease (PLD) with compression of surrounding structures, further worsening the clinical picture.[7] It is important to note that PLD can also manifest as an isolated condition, where 80% of patients are women, or as part of ADPKD.

ADPKD and gender

Epigenetics

Epigenetics studies heritable gene expression modifications, influenced by environmental and physiological factors. Key epigenetic modifications include DNA methylation, histone modifications, and non-coding RNAs. These mechanisms regulate transcriptional machinery access to genes, affecting gene expression variability. Epigenetics offers an additional layer of control, modulating gene activity in response to internal and external stimuli. In the context of ADPKD, earlier reports indicated that genetic imprinting may lead to a more severe form of the disease when inherited maternally rather than paternally; however, this is not universally supported by all studies.[14–16]

There is little concrete evidence that the severity of ADPKD is correlated with sex-based variations in epigenetic alterations. It is proposed for example that estrogens may be interact with epigenetic mechanisms to influence gene expression in females.[17,18] Although the current evidence remains limited, several potential pathways have been identified, listed in Table 1. However, further studies are needed to clarify these interactions and determine their impact on disease progression

Diagnosis

The diagnosis of ADPKD tends to be earlier in women for various clinical and biological reasons.[22,23]

Family history and screening: Women usually have greater awareness of their family history of genetic diseases, leading to more vigilant monitoring and earlier diagnostic testing.

Symptoms and clinical presentation: Women may exhibit more pronounced or severe symptoms at an earlier age compared to men. This can lead to a timelier diagnosis, as symptoms such as abdominal pain, hematuria, or urinary tract infections (UTIs) may prompt patients to seek medical assistance sooner.

Pregnancy: During pregnancy, ultrasounds are a routine examination crucial for monitoring fetal and maternal health. These examinations not only ensure a smooth pregnancy but can also detect renal anomalies, such as the presence of cysts or an overall increase in kidney size. The ultrasound diagnosis of ADPKD during

Table 1. Epigenetic mechanisms potentially influenced by estrogens in ADPKD.

Epigenetic mechanism	Estrogens interaction	Potential impact on gene expression	References
DNA methylation	Modulates DNMTs	Reduced expression of PDK1 gene and genes related to cystogenesis	19–21
Histone modifications	Modulates HATs, HDACs, HMTs, and HDMs	Regulating cell proliferation and ciliogenesis associated pathways	20
Non-coding RNAs	Influences miRNAs and lncRNAs	Modulate the expression of genes associated with renal fibrosis and inflammation	17,20

ADPKD: autosomal dominant polycystic kidney disease; DNMTs: DNA methyltransferases; HATs: histone acetyltransferases; HDACs: histone deacetylases; HDMs: histone demethylases; HMTs: histone methyltransferases.

pregnancy in pregnant women has been estimated at 2.41/10,000, compared to 1.49/10,000 in non-pregnant women aged 20–34.[22]

Disease manifestations

Regarding disease manifestations, it is known that women tend to more frequently experience chronic pain, macrohematuria, recurrent UTIs, and sometimes large hepatic cysts with organomegaly.[7,24,25] However, when considering the progression of renal failure, the female sex shows an advantage over the male sex, as the disease progression tends to be slower in women.[26–28]

The Predicting Renal Outcome in Polycystic Renal Disease score identifies male sex as a significant factor in renal failure progression.[29] Females seem to have protective effects on the average age of onset of end stage kidney disease (ESKD), as women generally begin renal replacement therapy 5.6 years later than men.[30] Recent Real-Life studies, such as the one conducted on a large Canadian cohort, have shown that men, as rapid progressors, have greater access to tolvaptan therapy and tend to initiate treatment earlier than women. Given the observed phenotypic differences and the different decline in renal function, it is natural to question the role of sex hormones in the development and progression of the disease.[31]

Specifically, it is necessary to explore how sex hormones may influence the pathological mechanisms underlying ADPKD, contributing to the differences in clinical manifestations and the rate of renal function deterioration between the sexes.[32]

Hormonal influences

Estrogens and the renin–angiotensin–aldosterone system. Activation of the renin–angiotensin–aldosterone system (RAAS) plays a crucial role in the development of hypertension in ADPKD and may accelerate renal disease progression. This occurs through a mitogenic mechanism mediated by angiotensin, promoting the growth of renal cysts.[13] Estrogens are also known to be potent suppressors of the RAAS. Thus, when estrogen levels significantly decrease, as happens during menopause, there can be a significant increase in RAAS activity.[26,33,34] The complex effects of estrogens include increased expression of the angiotensinogen gene, modification of renin concentrations, and an increase in vasodilators such as atrial natriuretic peptide.[26]

Estrogens generally decrease renin, angiotensin converting enzyme (ACE) activity, and angiotensinogen levels, while increasing AT(1) receptor density and aldosterone production. Progesterone competes with aldosterone for mineralocorticoid receptors. In contrast, the role of testosterone is less understood, but it appears to elevate renin levels and ACE activity.[35] The hormonal influences on the RAAS contribute to the sex-based disparities observed in cardiovascular and renal diseases.

Estrogens and renal function. Estrogens emerge as a protective factor against the progression of renal failure in women with ADPKD.[32,36] Estrogen receptors (ER-α and ER-β) play distinct and complex roles in the progression of cyst formation in both the kidneys and liver. Although both receptors are expressed in kidney tissue, ER-α appears to have a more prominent role in disease progression. Nonetheless, the relative expression levels and functional predominance of ER-α compared to ER-β in ADPKD tissues have yet to be conclusively determined.[37,38] ER-α has been implicated in promoting the growth of renal cysts, the activation of proliferative signaling like the MAPK/ERK pathway.[39] Also, in renal cysts, ER-α actives the mTOR pathway, which is heavily implicated in ADPKD cyst growth. And the receptor may upregulate cAMP signaling, a driver of cyst expansion in ADPKD.[40]

In contrast to ER-α, ER-β may have a more protective role: activation of ER-β has been shown to exert anti-proliferative and anti-fibrotic effects in kidney cells.[41] Recent findings have also demonstrated how estrogens have the opposite effect, suppressing RAAS axis and encouraging the upregulation of vascular endothelial growth factor (VEGF), protecting renal function, whereas male sex hormones promote the activation of the RAAS and the release of endothelin-1.[42]

It is also important to note that men are more prone to nephrolithiasis than women, and renal stones are known to

be a contributing factor to disease progression. The expression of osteopontin, a protective protein against kidney stones, is significantly influenced by estrogens.[43]

Recent studies have also focused on the importance of chloride channels, particularly calcium transmembrane channel 16A (TMEM16A), and the role of protein kinase A (PKA) in regulating these channels in ADPKD. PKA signaling is thought to regulate the activity of TMEM16A, which in turn modulates fluid secretion into cysts. This suggests that such mechanisms may represent therapeutic opportunities to limit the growth of renal cysts, especially in women.[44]

Moreover, women with ADPKD have decreased expression of the cystic fibrosis transmembrane conductance regulator (CFTR) because of estrogen-dependent regulation, whereas TMEM16A expression varies. Cyst development may be impacted by this reduction in CFTR.[45] Gender differences in renal calcium homeostasis are highlighted by recent studies that also show that differences in TMEM16A expression and hormonal regulation lead to a more severe phenotype in med with ADPKD, indicating that altered intracellular calcium levels may underlie cyst phenotype.[44]

Estrogens and hepatic cysts. While the frequency of hepatic involvement is similar in men and women, it tends to appear earlier and more severely in women. Hepatic cysts generally develop in women by the age of 60 depending on their estrogen levels during fertile period, especially in women with a history of pregnancies or those utilizing estrogen–progestin hormonal therapy.[7]

In fact, estrogens play a critical role in the development of hepatic cysts and the increase in liver volume[46]: estrogens directly influence gene transcription associated with cell proliferation by binding to cholangiocyte receptors, promoting cellular advancement via the p-ERK1/2 pathway. They also enhance proliferation through immune system interactions with macrophages and may affect angiogenesis through their interaction with VEGF.[37,47,48] Indirectly, estrogens stimulate the transcription and release of hepatocyte growth factor and insulin-like growth factor, enhancing cell growth.[49,50]

On the other hand, no research has shown that progesterone plays a major part in the development of hepatic cysts.

Menopause as a risk indicator. Menopause and ADPKD are interconnected, with hormonal changes during menopause impacting the progression and management of the disease. During menopausal transition, generally between the ages of 45 and 55, there is a crucial reduction in estrogen due to the cessation of ovarian function: this can lead to accelerated disease progression and a faster decline in kidney function, particularly as women age.[42,51] Reduced estrogen also increases the risk of other comorbidities, such as cardiovascular disease and metabolic changes.

Hormonal therapy

Considering the effect of estrogens on the growth of hepatic cysts, hormonal therapy has long been a subject of controversy in women with ADPKD, often being excluded a priori.

The therapeutic indications for hormonal therapy include conditions such as endometriosis, polycystic ovary syndrome (PCOS), dysmenorrhea, and contraception, primarily affecting women of reproductive age. Additionally, in menopausal women, hormonal therapy is used to manage vasomotor symptoms (VMS) and genitourinary syndrome, both of which can significantly impact quality of life.

In order of recommendation for women with ADPKD, in reproductive age the copper intrauterine device (IUD) is considered the safest and most suitable contraceptive method due to its non-hormonal nature and long duration, as mentioned in KDIGO guidelines.[25] Levonorgestrel IUDs are particularly useful for treating conditions such as endometriosis, endometrial hyperplasia. and abnormal uterine bleeding. Progestin-only contraceptives (POP) are a safer choice for ovulation inhibition, without administering estrogen to women. The vaginal ring may represent an acceptable option for those needing hormonal treatment for a limited period of time due to the escape of the first hepatic passage.[26]

Finally, while combined oral contraceptives (COCs) are effective in preventing ovulation and providing various non-contraceptive benefits, they are not recommended for patients with ADPKD. If their use is deemed clinically necessary, COCs should be prescribed only under close medical supervision and for the shortest duration possible.

In the context of menopause, the intricacies of ADPKD and the associated risks of hormonal therapy necessitate the importance of non-hormonal interventions in the management of menopause symptoms.[26]

Modifications in lifestyle, including dietary changes and consistent physical activity, can enhance overall well-being. Cognitive-behavioral therapies may assist women in managing mood disorders.

VMS may be partially managed with natural preparations; however, their efficacy is often limited, resulting in low patient compliance. Additional evidence indicates that the effectiveness of regular physical activity in reducing hot flashes.[52]

Genitourinary syndrome of menopause, primarily characterized by vulvovaginal atrophy, can significantly impact a woman's quality of life. It can be managed with hyaluronic acid-based ointments and lubricants. If these

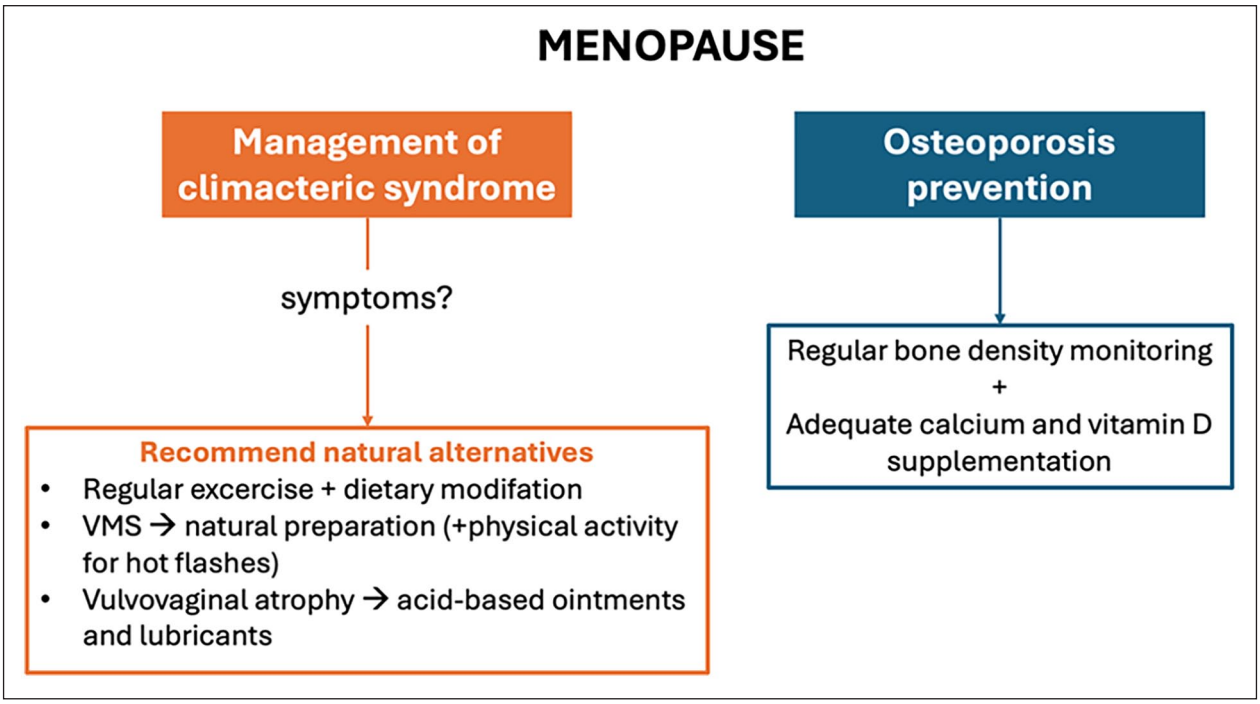

Figure 1. Menopause in ADPKD.
ADPKD: autosomal dominant polycystic kidney disease.

treatments prove ineffective, local estrogen therapy may be considered.

Adequate calcium and vitamin D supplementation, coupled with regular bone density monitoring, are critical elements of a comprehensive management strategy for preventing osteoporosis (Figure 1).

Tolvaptan and somatostatin analogs

By decreasing kidney volume and maintaining renal function, tolvaptan has been demonstrated in clinical trials to slow the progression of ADPKD. Recent studies have indicated that tolvaptan is equally effective in reducing renal volume and slowing the decline in GFR in both men and women.[53] Women may be more prone to side effects like pelvic organ prolapse or liver toxicity.[54] The enlargement of the kidneys results in increased intra-abdominal pressure, which weakens the pelvic floor muscles, a phenomenon that is more pronounced in patients with larger renal volumes. Furthermore, the significant diuresis caused by tolvaptan treatment leads to bladder distension, which further contributes to the weakening of these muscles.[55]

Tolvaptan is contraindicated during pregnancy. Although there is no enough information on humans, research on animals has revealed potential teratogenic. Women of childbearing potential should use effective contraception during treatment and for at least 1 month after discontinuation.[56]

Recent KDIGO guidelines recommend the use of long-acting somatostatin analog (SA) in individuals with ADPKD who have significantly enlarged polycystic livers causing severe volume-related symptoms.[25] Young women experience the greatest benefit from treatment with SA on liver volume decrease in contrast to men. Studies suggest estrogens may enhance SAs' ability to inhibit cyclic adenosine monophosphate production in cholangiocytes, increasing susceptibility to SA therapy in fertile women.[57]

PCOS: Is there a correlation with ADPKD?

ADPKD and PCOS are distinct conditions, with common features, suggesting potential genetic and metabolic factors.

PCOS is a endocrine-metabolic disorder affecting about 20% of women of reproductive age. According to the Rotterdam criteria, a diagnosis requires at least two of the following three criteria: oligo-ovulation and/or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries.[58]

The etiopathogenesis of PCOS is multifactorial, involving genetic and environmental mechanisms.[59,60] DKK1 and DNAJB1 are potentially relevant in PCOS pathogenesis, with DKK1 overexpressed in ovarian cells and DNAJB1 involved in androgen signaling processes.[61–65]

PCOS manifests with the presence of multiple ovarian cysts, which can contribute to hormonal and reproductive dysfunctions.[60] While there is currently no definitive

evidence directly linking ADPKD genes to PCOS, interest in potential genetic interactions and common risk factors is increasing. Some studies suggest that genetic mutations associated with ADPKD could increase the risk of developing PCOS. This potential genetic overlap raises questions about whether the presence of one condition may predispose individuals to the other.[61,66]

Insulin resistance appears to be another common factor in both ADPKD and PCOS, albeit in different ways. Insulin resistance is present in many women with PCOS and plays a key role in the syndrome's pathogenesis by stimulating hyperandrogenism. Insulin resistance leads to a compensatory state of hyperinsulinemia, which in turn stimulates ovarian hyperandrogenism, a hallmark of PCOS.[67] While less studied in relation to PCOS, insulin resistance also seems to be a common factor in patients with ADPKD.[68]

The possible link between ADPKD and PCOS represents an intriguing area of study. Although definitive evidence of clear pathogenic connections between these two conditions is still lacking, exploring their interactions may provide important insights into their development and management.

Fertility

In women with ADPKD who have normal kidney function, fertility is not altered.[69] However, in men, fertility may be slightly compromised due to sperm abnormalities or the presence of cysts in the distal seminal tract.[70,71]

Women with ADPKD tend to have fewer pregnancies. In fact, only 45% of patients of childbearing age express the intention to have children, and this number decreases further in women with pre-existing CKD.[72]

This reduced inclination toward motherhood is primarily related to concerns about the hereditary nature of the disease. The average age at first childbirth is similar between women with ADPKD and the general population. However, ADPKD patients tend to have an average of only one pregnancy, compared to the general population.[73]

Pregnancy

Pregnancies in women with ADPKD should be closely monitored at a specialized referral center by a multidisciplinary team of experienced gynecologists and nephrologists.

Maternal–fetal outcomes. Pregnant women with CKD are known to have a higher risk of adverse outcomes for both the mother and fetus compared to women with normal kidney function.[74] However, the specific influence of ADPKD on pregnancy remains uncertain, and the number of available studies on this topic is limited. For women with ADPKD who have normal BP and kidney function, pregnancy outcomes are typically favorable and comparable to those observed in the general population.[75–77]

Pre-existing CKD, hypertension, and advanced maternal age are recognized as unfavorable fetal outcomes in many renal diseases.[78–81] Additionally, compared to hypertensive women of the same age, ADPKD women who have had more than three pregnancies seem to exhibit decreased renal function as they age.[75] The development of preeclampsia in ADPKD patients is closely correlated with an earlier onset of chronic hypertension.[82] Approximately one-quarter of pregnant women experience hypertensive complications: 16% develop gestational hypertension, while 11% experience preeclampsia.[75]

According to a retrospective research, women with ADPKD had a somewhat greater incidence of preterm delivery and intrauterine growth restriction than healthy controls; however, these results were not statistically significant and are still isolated cases.[73] Chronic hypertension established before to pregnancy as in ADPKD, that is inadequately managed during gestation is linked to an increased risk of preterm birth; thus, meticulous monitoring is advised.[83] The rates of miscarriage and fetal mortality in the ADPKD population did not differ significantly from those in the general population.

Another significant complication related to ADPKD during pregnancy is the increased risk of thromboembolism. The enlargement of the kidneys, especially the right kidney, and the liver may compress the iliac veins and the inferior vena cava, increasing the risk of thrombosis and pulmonary embolism. This risk is further amplified by the pro-coagulant state typical of pregnancy.[84–86] General clinical guidelines for pregnancy recommend the use of a low dose of aspirin (75–150 mg daily) to reduce the risk of preeclampsia in women with CKD.[87] In KDIGO ADPKD guidelines low-dose aspirin is recommended from weeks 12 to 36.[25] However, the use of aspirin should be carefully evaluated due to the increased risk of bleeding, particularly in women with cerebral aneurysms or recurrent episodes of cystic hemorrhage. Consequently, the decision to use aspirin must be personalized and based on an assessment of individual risks.

Women with ADPKD also present a higher risk of ectopic pregnancies, suggesting possible structural alterations in the fallopian tubes.[88]

Additionally, ADPKD is associated with an increased incidence of UTIs during pregnancy. For this reason, antibiotic prophylaxis is recommended for women with ADPKD following a single confirmed episode of UTI, even in the absence of symptoms, to prevent further complications during pregnancy.[25,87]

Counseling. When women with ADPKD plan a pregnancy, they face complex decisions regarding not only their health but also the future of their offspring, including the potential hereditary transmission of the disease. These decisions

are influenced by the expectations of partners and families, and sometimes concern about risks may overshadow hope, leading to renunciations.[89]

Preconception counseling must address various aspects, including the optimization of pharmacological therapy, reproductive options, potential pregnancy outcomes, and risks for both mother and child. Furthermore, it is essential to evaluate the long-term impact of pregnancy on renal and cardiovascular health, as well as the potential implications for PLD.[25,90]

A personalized risk assessment, considering renal function, proteinuria, and BP, is thus fundamental. Additionally, performing a renal ultrasound can be useful for monitoring cyst progression, especially if it has not been recently conducted.

A crucial aspect of pregnancy for women with ADPKD is the hereditary nature of the disease. For conditions with a high probability of transmission, assisted reproductive technologies represent a viable option for patients wishing to have healthy children.[7,72,90] Third-generation in vitro fertilization (IVF) and preimplantation genetic testing (PGT) have been successfully used to reduce the risk of transmitting ADPKD to offspring, bringing the probability of transmission down from 50% to 1%–2%.[91]

However, PGT is only possible if the disease-causing mutation has been identified in the family and a single-cell genetic test has been developed. In some families affected by ADPKD, the complexity of variable penetrance caused by polymorphic alleles and modifier variants may complicate genetic counseling and make PGT impossible.[92] Despite these limitations, PGT offers a personalized approach to managing the inheritance of this chronic and potentially debilitating condition.

Furthermore, IVF carries risks such as a slight increase in the risk of ovarian hyperstimulation syndrome, ectopic pregnancies, and potential progression of PLD due to estrogen-based medication.[92] Although estrogen-based medication is commonly used in IVF procedures, their usage in women with ADPKD should be carefully considered. In this situation, having a comprehensive conversation with medical professionals and taking into account individualized treatment plans are crucial first steps in reducing the hazards connected to estrogen medication.[93]

PLD and transplantation

Only 10%–20% of patients with PLD characterized by multiple cysts and hepatomegaly exhibit significant clinical symptoms, with most of these patients being women. The volume of the liver has a significant impact on prognosis, especially when associated with frequent hospitalizations and refractory symptoms that severely compromise the patient's quality of life and overall well-being. Organomegaly is often accompanied by malnutrition and esophageal and gastric symptoms, such as dyspnea, reflux, massive ascites, and abdominal pain. Major risk factors include female sex, multiple pregnancies, and prolonged estrogen therapy.[7,26]

Most patients require clinical treatment, primarily pharmacological, aimed at alleviating symptoms. Liver transplantation represents the last therapeutic option for selected cases of ADPKD and severe PLD that do not respond to other therapies. This solution becomes particularly relevant for patients in ESKD or advanced stages (stage 3b–4) who also require a kidney transplant, making combined transplantation feasible.[94]

In some countries, organ allocation is based solely on the Model for End-Stage Liver Disease (MELD) score, which does not adequately reflect the severity of liver disease in PLD cases. Even in severe PLD, good liver function and protein synthesis are maintained, with no alteration of classic markers of liver dysfunction, such as prothrombine time (PT) and serum albumin, which significantly contribute to the MELD score. Consequently, the priority on the transplant waiting list is often low.[7]

Currently, there are no universally accepted objective indications for liver transplantation in ADPKD cases, and each case must be evaluated individually. Transplantation is usually reserved for patients who do not respond to other therapies or who experience progressive deterioration of liver function, although this is rare.

Despite the fortunate increase in double kidney–liver transplants in recent years, objective guidelines defining indications for the procedure are lacking. The absence of standardized protocols and severity criteria limits the ability to accurately identify ideal candidates. Although no indication criteria based solely on organ size exist, they must be considered a crucial factor, especially in female patients, due to their significant impact on quality of life. Besides metabolic complications, gastrointestinal and respiratory symptoms, along with psychological aspects, are crucial factors that need to be addressed to improve the overall well-being of patients.

When well indicated, double kidney–liver transplantation offers excellent outcomes in terms of survival and quality of life improvement, although this indication remains relatively uncommon.[94]

Psychological aspects

From a psychological perspective, women with ADPKD face a series of specific challenges, in addition to the common symptoms experienced by all patients with this disease. Scientific research and clinical experience have highlighted that these women must confront not only the debilitating physical symptoms of the disease but also profound psychological repercussions related to their body image and quality of life.[95]

One of the most significant physical issues is the development of an enlarged abdomen due to the expansion of

renal cysts and, in some cases, hepatic cysts. This abdominal enlargement leads to chronic and uncomfortable bloating, often accompanied by pain, which limits the patients' movements and daily activities. However, the discomfort extends beyond the physical: the appearance of a distended abdomen, which may make them look pregnant, negatively impacts how women perceive their bodies, leading to embarrassment and insecurity.[96]

This discomfort related to body image significantly affects their self-esteem and quality of life, influencing not only social relationships but also intimate ones. In particular, many women report difficulties in the sexual sphere and problems with interaction within the couple, a phenomenon that, while it can also occur in men with ADPKD, is particularly felt by women.[96]

Another major concern for women with ADPKD is family planning. The fear of passing the disease onto their children is often a source of anxiety and indecision. Pregnancy, already a complex period in a woman's life, becomes even more delicate for these patients, who must face not only the biological and physiological changes typical of this phase but also a significant emotional and psychological burden.

Concerns primarily revolve around the risk of complications related to the disease, such as worsening renal function, the development of pregnancy-induced hypertension, and preeclampsia—conditions that can accelerate progression toward ESKD. This fear for the future, combined with the possibility of transmitting the disease, can make pregnancy a particularly stressful and anxiety-laden experience.[97]

In general, while pregnancy is often idealized as a period of unconditional happiness, for women with ADPKD, it can represent an extremely challenging phase, both physically and emotionally. These factors underscore the importance of targeted psychological support that considers the specific needs of these patients, helping them manage the complexities of their condition and improve their overall quality of life. Women with ADPKD often experience profound feelings of frustration, confusion, and stress related to the fear of genetically transmitting the disease to their children. This fear is accompanied by a higher risk of fetal loss, as evidenced by recent studies.[73,95] These concerns can generate a wide range of psychological distress, both during pregnancy and in the postpartum period.

Moreover, these issues can significantly impact the couple's relationship, creating tensions and difficulties in communication and intimacy with their partner. These elements highlight the importance of adequate and timely psychological support for women with ADPKD, especially during and after pregnancy.

Among the psychological intervention models used to reduce psychophysical distress caused by illness, body-based approaches have proven effective. Mindfulness protocols have a positive impact on psychophysical distress. These programs aim to enhance self-awareness and self-acceptance, guiding individuals through a process of self-discovery. The goal is to help patients understand their physical illness and develop a healthier, more functional relationship with both their bodies and their condition.

For these interventions to be effective, patients must be actively engaged. This can be achieved, for example, through open communication with the care team and the doctor, who serves as a point of reference during treatment.[98]

Women in our outpatient clinic

About five new diagnoses are made each month at the San Raffaele Hospital's dedicated ADPKD clinic, which has been in operation for 15 years and currently has 400 patients in follow-up from all over Italy. Over 200 patients are female, and as shown in Figure 2, they are the focus of a treatment plan specifically designed for them that utilizes some significant partnerships.

If a woman feels the need for psychological support, or if it is deemed helpful, a dedicated pathway for mental healthcare can be initiated. This often includes focused work on body image concerns, which can arise due to changes in physical appearance or health status related to ADPKD, and also on the dynamics of the couple's relationship.

Many women with ADPKD develop unhealthy eating habits due to emotional eating, erratic appetite, and managing the condition. Working with a nutritionist can help transform these habits. Insulin resistance is more likely in ADPKD patients, and a well-planned, kidney-friendly diet with low glycemic index, low-sodium, and balanced approach is crucial for long-term health.

Conclusions

Most of the literature to date has concentrated on ADPKD as a general condition, there is mounting evidence that suggests women may differ from men in terms of how the disease progresses, how they respond to treatment, and how they fare overall. Caring for women with ADPKD requires a compassionate, personalized approach that considers genetic, physical, and emotional dimensions of the disease.

Woman's genetic profile does not include only PDK1 or PDK2 mutations, but also genetic modifiers. These genetic differences can offer valuable information about how each patient's disease will progress, enabling more individualized and efficient treatments. Plans for treatment can be modified to better manage the illness and enhance results by taking genetic information into account.

Early genetic counseling can provide valuable insights for family planning and help clarify the potential impact of the disease.

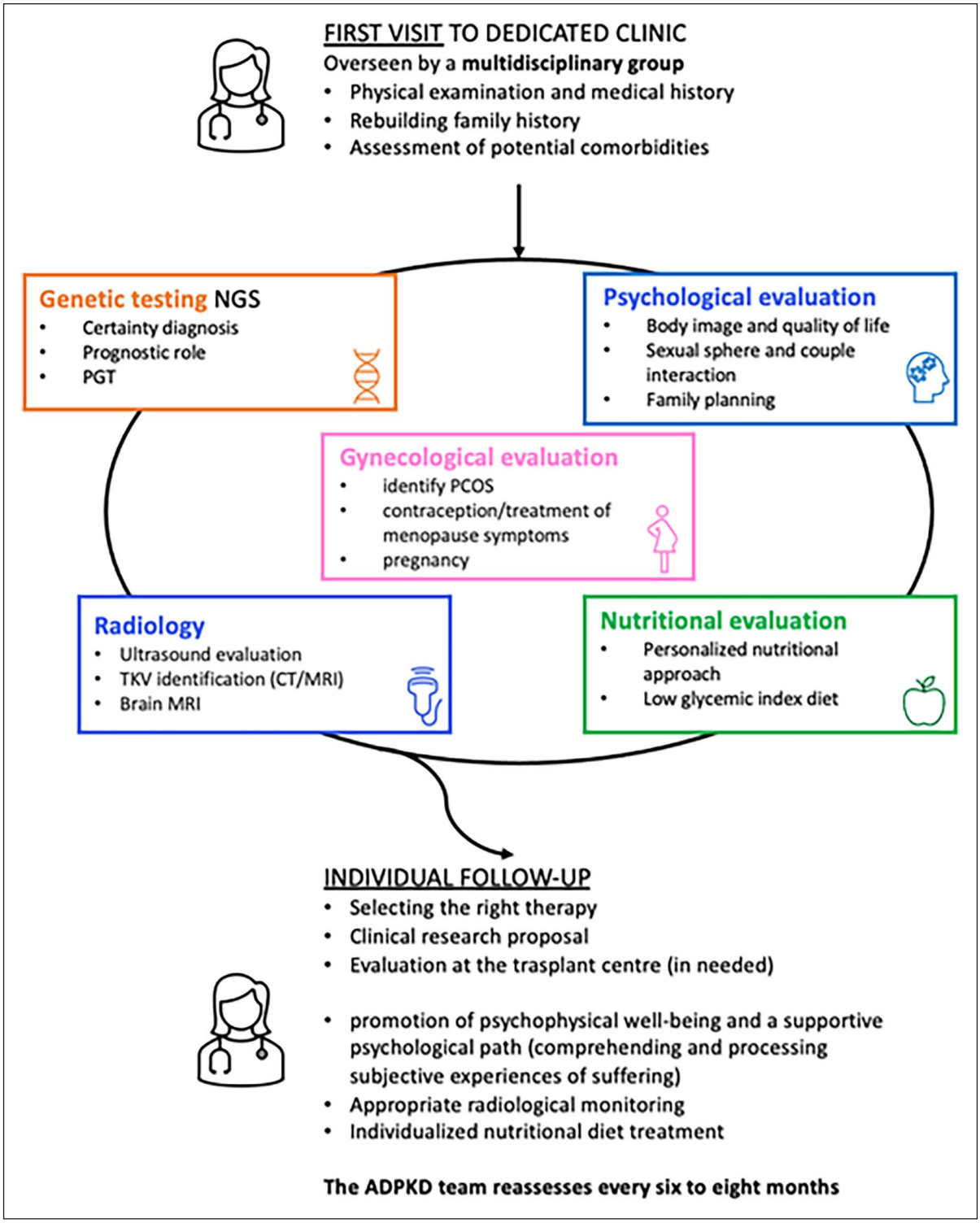

Figure 2. Multidisciplinary approach in ADPKD.
ADPKD: autosomal dominant polycystic kidney disease; CT: computed tomography; MRI: magnetic resonance imaging; NGS: next-generation sequencing; PCOS: polycystic ovary syndrome; TKV: total kidney volume.

Women with ADPKD frequently experience symptoms like abdominal pain, hematuria, and recurrent UTIs more intensely. Imaging, such as ultrasound, MRI, or computed tomography, is essential to evaluate cyst burden in both kidneys and liver, as liver involvement is often more prevalent in women.

Hormonal pathways play an important part in ADPKD as well. Hormonal changes in women, particularly during pregnancy and menopause, can affect kidney function and cyst development. In order to ensure that women receive care that is appropriate for their stage of life, treatment, and counseling are informed by an understanding of these hormonal interactions.

Pregnancy counseling is crucial due to ADPKD's genetic implications and associated maternal-fetal risks. For those considering family planning, PGT is a valuable option. When discussing contraception, non-hormonal methods such as the copper IUD, or minimally systemic hormonal options like the vaginal ring, can help limit estrogen's effect on liver cyst growth. Menopause introduces additional challenges and non-hormonal treatments or local hormone therapy are the most recommended.

For women with significant liver symptoms, lifestyle modifications may offer some benefit, while severe cases may require liver transplant consideration. The psychological impact of ADPKD is profound, affecting body image, self-esteem, and hereditary concerns. Ongoing psychological support is crucial to address these issues, and a collaborative, individualized care plan can empower women to manage ADPKD with confidence and resilience. By addressing both physical and emotional aspects, we can help women navigate ADPKD with a greater sense of control and well-being, supporting a better quality of life.

Limitation of the study

This review has several limitations. Restricting inclusion to studies from selected databases may have introduced selection bias. The included studies varied in quality, with some lacking methodological rigor, which may affect the strength of the conclusions. Significant heterogeneity in populations, interventions, and outcomes limited the ability to conduct a meta-analysis.

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Ethical considerations

This narrative review adheres to the ethical guidelines and no primary data involving human participants were collected.

Consent for publication

By submitting this article, the authors confirm that they have obtained the necessary permissions for publication.

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References

1. Samulowitz A, Gremyr I, Eriksson E, et al. "Brave men" and "emotional women": a theory-guided literature review on gender bias in health care and gendered norms towards

patients with chronic pain. *Pain Res Manag* 2018; 2018: 6358624.
2. Gender disparities in clinical decision making. Council on Ethical and Judicial Affairs, American Medical Association. *JAMA* 1991; 266(4): 559–562.
3. Bucci R, de Rosa LI, Pisoni MB, et al. The management of patients with adult autosomal dominant polycystic kidney disease (ADPKD) requires a multidisciplinary approach. *G Ital Nefrol* 2023; 40(6): 2023.
4. Solazzo A, Testa F, Giovanella S, et al. The prevalence of autosomal dominant polycystic kidney disease (ADPKD): a meta-analysis of European literature and prevalence evaluation in the Italian province of Modena suggest that ADPKD is a rare and underdiagnosed condition. *PLoS One* 2018; 13(1): e0190430.
5. Pippias M, Kramer A, Noordzij M, et al. The European Renal Association—European Dialysis and Transplant Association Registry annual report 2014: a summary. *Clin Kidney J* 2017; 10(2): 154–169.
6. Bergmann C, Guay-Woodford LM, Harris PC, et al. Polycystic kidney disease. *Nat Rev Dis Primers* 2018; 4(1): 50.
7. Chapman AB, Devuyst O, Eckardt KU, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2015; 88(1): 17–27.
8. Kim DY and Park JH. Genetic mechanisms of ADPKD. *Adv Exp Med Biol* 2016; 933: 13–22.
9. Chang AR, Moore BS, Luo JZ, et al. Exome sequencing of a clinical population for autosomal dominant polycystic kidney disease. *JAMA* 2022; 328(24): 2412–2421.
10. Cornec-Le Gall E, Torres VE and Harris PC. Genetic complexity of autosomal dominant polycystic kidney and liver diseases. *J Am Soc Nephrol* 2018; 29(1): 13–23.
11. Senum SR, Li YSM, Benson KA, et al. Monoallelic IFT140 pathogenic variants are an important cause of the autosomal dominant polycystic kidney-spectrum phenotype. *Am J Hum Genet* 2022; 109(1): 136–156.
12. Cornec-Le Gall E, Audrézet MP, Chen JM, et al. Type of PKD1 mutation influences renal outcome in ADPKD. *J Am Soc Nephrol* 2013; 24(6): 1006–1013.
13. Hian CK, Lee CL and Thomas W. Renin-angiotensin-aldosterone system antagonism and polycystic kidney disease progression. *Nephron* 2016; 134(2): 59–63.
14. Choukroun G, Itakura Y, Albouze G, et al. Factors influencing progression of renal failure in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1995; 6(6): 1634–1642.
15. Bear JC, Parfrey PS, Morgan JM, et al. Autosomal dominant polycystic kidney disease: new information for genetic counselling. *Am J Med Genet* 1992; 43(3): 548–553.
16. Nowak KL, Chonchol M, You Z, et al. Affected parent sex and severity of autosomal dominant polycystic kidney disease: a retrospective cohort study. *Clin Nephrol* 2018; 89(3): 196–204.
17. Kumar P and Brooks HL. Sex-specific epigenetic programming in renal fibrosis and inflammation. *Am J Physiol Renal Physiol* 2023; 325(5): F578–F594.
18. Li X. Epigenetics and cell cycle regulation in cystogenesis. *Cell Signal* 2020; 68: 109509.
19. Woo YM, Bae JB, Oh YH, et al. Genome-wide methylation profiling of ADPKD identified epigenetically regulated genes associated with renal cyst development. *Hum Genet* 2014; 133(3): 249–263.
20. Agborbesong E, Li LX, Li L, et al. Molecular mechanisms of epigenetic regulation, inflammation, and cell death in ADPKD. *Front Mol Biosci* 2022; 9: 922428.
21. Hajirezaei F, Ghaderian SMH, Hasanzad M, et al. Methylation of the PKD1 promoter inversely correlates with its expression in autosomal dominant polycystic kidney disease. *Rep Biochem Mol Biol* 2020; 9(2): 193–198.
22. Willey C, Kamat S, Stellhorn R, et al. Analysis of nationwide data to determine the incidence and diagnosed prevalence of autosomal dominant polycystic kidney disease in the USA: 2013–2015. *Kidney Dis* 2019; 5(2): 32–45.
23. Courtenay WH. Constructions of masculinity and their influence on men's well-being: a theory of gender and health. *Soc Sci Med* 2000; 50(10): 126–138.
24. Hogan MC and Norby SM. Evaluation and management of pain in autosomal dominant polycystic kidney disease. *Adv Chronic Kidney Dis* 2010; 17(3): e1–e16.
25. Devuyst O, Ahn C, Barten TRM, et al. KDIGO 2025 clinical practice guideline for the evaluation, management, and treatment of autosomal dominant polycystic kidney disease (ADPKD). *Kidney Int* 2025; 107(2): S1–S239.
26. Petrone M, Catania M, De Rosa LI, et al. Role of female sex hormones in ADPKD progression and a personalized approach to contraception and hormonal therapy. *J Clin Med* 2024; 13(5): 1257.
27. Grantham JJ, Torres VE, Chapman AB, et al. Volume progression in polycystic kidney disease. *N Engl J Med* 2006; 354(20): 112–118.
28. Corradi V, Gastaldon F, Caprara C, et al. Predictors of rapid disease progression in autosomal dominant polycystic kidney disease. *Minerva Med* 2017; 108(1): 43–56.
29. Cornec-Le Gall E, Audrézet MP, Rousseau A, et al. The PROPKD score: a new algorithm to predict renal survival in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 2016; 27(3): 942–951.
30. Ishikawa I, Maeda K, Nakai S, et al. Gender difference in the mean age at the induction of hemodialysis in patients with autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 2000; 35(6): 38–52.
31. Neugarten J and Golestaneh L. Gender and the prevalence and progression of renal disease. *Adv Chronic Kidney Dis* 2013; 20(5): 390–395.
32. Gava AL, Freitas FPS, Meyrelles SS, et al. Gender-dependent effects of aging on the kidney. *Braz J Med Biol Res* 2011; 44(9): 905–913.
33. Komukai K, Mochizuki S and Yoshimura M. Gender and the renin–angiotensin–aldosterone system. *Fundam Clin Pharmacol* 2010; 24(6): 687–698.
34. Xue B, Johnson AK and Hay M. Sex differences in angiotensin II- and aldosterone-induced hypertension: the central protective effects of estrogen. *Am J Physiol Regul Integr Comp Physiol* 2013; 305(5): R459–R463.
35. O'Donnell E, Floras JS and Harvey PJ. Estrogen status and the renin angiotensin aldosterone system. *Am J Physiol Regul Integr Comp Physiol* 2014; 307: 120–132.

36. Pechere-Bertschi A and Burnier M. Gonadal steroids, salt-sensitivity and renal function. *Curr Opin Nephrol Hypertens* 2007; 16(1): 16–21.
37. Aapkes SE, Bernts LHP, Barten TRM, et al. Estrogens in polycystic liver disease: a target for future therapies?. *Liver Int* 2021; 41(9): 2009–2019.
38. Ma HY, Chen S and Du Y. Estrogen and estrogen receptors in kidney diseases. *Ren Fail* 2021; 43(1): 619–642.
39. Tian W, Zhang Z and Cohen DM. MAPK signaling and the kidney. *Am J Physiol Renal Physiol* 2000; 279(4): F593–F604.
40. Strazzabosco M and Somlo S. Polycystic liver diseases: congenital disorders of cholangiocyte signaling. *Gastroenterology* 2011; 140(7): 85–102.
41. Cao R, Su W, Sheng J, et al. Estrogen receptor β attenuates renal fibrosis by suppressing the transcriptional activity of Smad3. *Biochim Biophys Acta Mol Basis Dis* 2023; 1869(6): 166755.
42. Conte C, Antonelli G, Melica ME, et al. Role of sex hormones in prevalent kidney diseases. *Int J Mol Sci* 2023; 24: 38–52.
43. Heller HJ, Sakhaee K, Moe OW, et al. Etiological role of estrogen status in renal stone formation. *J Urol* 2002; 168(5): 142–156.
44. Talbi K, Cabrita I, Schreiber R, et al. Gender-dependent phenotype in polycystic kidney disease is determined by differential intracellular Ca^{2+} signals. *Int J Mol Sci* 2021; 22(11): 6019.
45. Saint-Criq V and Harvey BJ. Estrogen and the cystic fibrosis gender gap. *Steroids* 2014; 81: 124–132.
46. Sherstha R, McKinley C, Russ P, et al. Postmenopausal estrogen therapy selectively stimulates hepatic enlargement in women with autosomal dominant polycystic kidney disease. *Hepatology* 1997; 26(5): 98–120.
47. Fatima LA, Campello RS, Santos RDS, et al. Estrogen receptor 1 (ESR1) regulates VEGFA in adipose tissue. *Sci Rep* 2017; 7(1): 166–178.
48. Kovats S. Estrogen receptors regulate innate immune cells and signaling pathways. *Cell Immunol* 2015; 294(2): 63–69.
49. Alvaro D, Mancino MG, Onori P, et al. Estrogens and the pathophysiology of the biliary tree. *World J Gastroenterol* 2006; 12(22): 3537–3545.
50. Alvaro D, Alpini G, Onori P, et al. Alfa and beta estrogen receptors and the biliary tree. *Mol Cell Endocrinol* 2002; 193(1–2): 105–108.
51. Vellanki K and Hou S. Menopause in CKD. *Am J Kidney Dis* 2018; 71(5): 710–719.
52. Franco OH, Chowdhury R, Troup J, et al. Use of plant-based therapies and menopausal symptoms: a systematic review and meta-analysis. *JAMA* 2016; 315(23): 2554–2563.
53. Yamazaki M, Kawano H, Miyoshi M, et al. Long-term effects of tolvaptan in autosomal dominant polycystic kidney disease: predictors of treatment response and safety over 6 years of continuous therapy. *Int J Mol Sci* 2024; 25(4): 2088.
54. Hammond S, Meng X, Barber J, et al. Tolvaptan safety in autosomal-dominant polycystic kidney disease; a focus on idiosyncratic drug-induced liver injury liabilities. *Toxicol Sci* 2025; 203(1): 11–27.
55. Sango C, Merino Bueno MDC, Gallardo Pérez A, et al. Pelvic organ prolapse in women with autosomal dominant polycystic kidney disease under tolvaptan treatment. *Nefrologia* 2023; 43(6): 791–792.
56. Gittus M, Haley H, Harris T, et al. Commentary: tolvaptan for autosomal dominant polycystic kidney disease (ADPKD)—an update. *BMC Nephrol* 2025; 26(1): 79.
57. Gevers TJG, Inthout J, Caroli A, et al. Young women with polycystic liver disease respond best to somatostatin analogues: a pooled analysis of individual patient data. *Gastroenterology* 2013; 145(2): 357–365.e1–e2.
58. Fauser BCJM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril* 2004; 81(1): 45–62.
59. Patel S. Polycystic ovary syndrome (PCOS), an inflammatory, systemic, lifestyle endocrinopathy. *J Steroid Biochem Mol Biol* 2018; 182: 27–36.
60. Yang J and Chen C. Hormonal changes in PCOS. *J Endocrinol* 2024; 261(1): e230342.
61. Abdul-Majeed S and Nauli SM. Polycystic diseases in visceral organs. *Obstet Gynecol Int* 2011; 2011: 609370.
62. Kahsar-Miller MD, Nixon C, Boots LR, et al. Prevalence of polycystic ovary syndrome (PCOS) in first-degree relatives of patients with PCOS. *Fertil Steril* 2001; 75(1): 53–58.
63. Legro RS, Driscoll D, Strauss JF, et al. Evidence for a genetic basis for hyperandrogenemia in polycystic ovary syndrome. *Proc Natl Acad Sci U S A* 1998; 95(25): 14956–14960.
64. Bruni V, Capozzi A and Lello S. The role of genetics, epigenetics and lifestyle in polycystic ovary syndrome development: the state of the art. *Reprod Sci* 2022; 29(3): 668–679.
65. Jones MR, Chua A, Chen YDI, et al. Harnessing expression data to identify novel candidate genes in polycystic ovary syndrome. *PLoS One* 2011; 6(5): e20120.
66. Braun JEA. Extracellular chaperone networks and the export of J-domain proteins. *J Biol Chem* 2023; 299(2): 102840.
67. Xu Y and Qiao J. Association of insulin resistance and elevated androgen levels with polycystic ovarian syndrome (PCOS): a review of literature. *J Healthc Eng* 2022; 2022: 9240569.
68. Chirumamilla R, Mina D, Siyahian S, et al. Subclinical metabolic and cardiovascular abnormalities in autosomal dominant polycystic kidney disease. *Clin Nephrol* 2018; 90(4): 138–152.
69. Vora N, Perrone R and Bianchi DW. Reproductive issues for adults with autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 2008; 51(2): 307–318.
70. Kanagarajah P, Ayyathurai R and Lynne CM. Male infertility and adult polycystic kidney disease—revisited: case report and current literature review. *Andrologia* 2012; 44(suppl 1): 162–178.
71. Belet U, Danaci M, Sarikaya Ş, et al. Prevalence of epididymal, seminal vesicle, prostate, and testicular cysts in autosomal dominant polycystic kidney disease. *Urology* 2002; 60(1): 212–222.
72. Sun M, Xue C, Lu Y, et al. The fertility willingness and acceptability of preimplantation genetic testing in Chinese patients with autosomal dominant polycystic kidney disease. *BMC Nephrol* 2020; 21(1): 68–89.

73. Wu M, Wang D, Zand L, et al. Pregnancy outcomes in autosomal dominant polycystic kidney disease: a case–control study. *J Matern Fetal Neonatal Med* 2016; 29(5): 807–812.
74. Gabow PA, Johnson AM, Kaehny WD, et al. Factors affecting the progression of renal disease in autosomal-dominant polycystic kidney disease. *Kidney Int* 1992; 41(5): 89–110.
75. Chapman AB, Johnson AM and Gabow PA. Pregnancy outcome and its relationship to progression of renal failure in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1994; 5(5): 1178–1185.
76. Schrier RW, Brosnahan G, Cadnapaphornchai MA, et al. Predictors of autosomal dominant polycystic kidney disease progression. *J Am Soc Nephrol* 2014; 25(11): 2399–2418.
77. Jung JH, Kim MJ, Lim HJ, et al. Successful pregnancy in a patient with autosomal dominant polycystic kidney disease on long-term hemodialysis. *J Korean Med Sci* 2014; 29(2): 301–304.
78. Hui D and Hladunewich MA. Chronic kidney disease and pregnancy. *Obstet Gynecol* 2019; 133(6): 211–215.
79. Agrawal A and Wenger NK. Hypertension during pregnancy. *Curr Hypertens Rep* 2020; 22(9): 64.
80. Gupta S, Petras L, Tufail MU, et al. Hypertension in pregnancy: what we now know. *Curr Opin Nephrol Hypertens* 2023; 32(2): 153–164.
81. Vakilzadeh N, Legardeur H, Desseauve D, et al. Pregnancy and chronic renal failure: what is new in 2023?. *Rev Med Suisse* 2023; 19(816): 401–405.
82. McBride L, Wilkinson C and Jesudason S. Management of autosomal dominant polycystic kidney disease (ADPKD) during pregnancy: risks and challenges. *Int J Womens Health* 2020; 12: 409–422.
83. Delker E, Bandoli G, LaCoursiere Y, et al. Chronic hypertension and risk of preterm delivery: National Longitudinal Study of Adolescents to Adult Health. *Paediatr Perinat Epidemiol* 2022; 36(3): 370–379.
84. Basheer M, Saad E and Assy N. Pulmonary embolism in autosomal dominant polycystic kidney patient induced by inferior vena cava mechanical compression. *Eur J Case Rep Intern Med* 2021; 8(8): 002767.
85. Badejoko OO, Dada OF, Ubom AE, et al. Suspected pulmonary embolism postcesarean section in a patient with autosomal dominant polycystic kidney disease. *Niger Med J* 2020; 61(4): 223–225.
86. Yin X, Blumenfeld JD, Riyahi S, et al. Prevalence of inferior vena cava compression in ADPKD. *Kidney Int Rep* 2021; 6(1): 168–178.
87. Wiles K, Chappell L, Clark K, et al. Clinical practice guideline on pregnancy and renal disease. *BMC Nephrol* 2019; 20(1): 401.
88. Milutinovic J, Fialkow PJ, Agodoa LY, et al. Fertility and pregnancy complications in women with autosomal dominant polycystic kidney disease. *Obstet Gynecol* 1983; 61(5): 68–92.
89. Tong A, Brown MA, Winkelmayer WC, et al. Perspectives on pregnancy in women with CKD: a semistructured interview study. *Am J Kidney Dis* 2015; 66(6): 210–220.
90. Zhou C, Mei C and Xue C. Preimplantation genetic diagnosis of autosomal dominant polycystic kidney disease applied in China. *Am J Kidney Dis* 2018; 72: 128–135.
91. Murphy EL, Droher ML, DiMaio MS, et al. Preimplantation genetic diagnosis counseling in autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 2018; 72(6): 135–152.
92. Kawwass JF and Badell ML. Maternal and fetal risk associated with assisted reproductive technology. *Obstet Gynecol* 2018; 132(3): 763–772.
93. Campbell RE, Edelstein CL and Chonchol M. Overview of ADPKD in pregnancy. *Kidney Int Rep* 2025; 10(4): 1011–1019.
94. Kirchner GI, Rifai K, Cantz T, et al. Outcome and quality of life in patients with polycystic liver disease after liver or combined liver-kidney transplantation. *Liver Transpl* 2006; 12(8): 1268–1277.
95. Baker A, King D, Marsh J, et al. Understanding the physical and emotional impact of early-stage ADPKD: experiences and perspectives of patients and physicians. *Clin Kidney J* 2015; 8(5): 145–163.
96. Delli Zotti GB, Sangiovanni E, Brioni E, et al. Psychological assessment of a sample of women with ADPKD: quality of life, body image, anxiety and depression. *G Ital Nefrol* 2019; 36(2): 2019.
97. Clarke A, Sarangi S and Verrier-Jones K. Voicing the lifeworld: parental accounts of responsibility in genetic consultations for polycystic kidney disease. *Soc Sci Med* 2011; 72(11): 1743–1751.
98. Bara BG. *Il corpo malato—L'intervento psicologico*. Raffaello Cortina Editore (ed), Milano. 2023.