



Hereditary and rare nephropathies

ORIGINAL ARTICLE

Understanding the physical and emotional impact of early-stage ADPKD: experiences and perspectives of patients and physicians

Anna Baker¹, Dominic King², James Marsh³, Andrew Makin⁴, Alison Carr⁵, Catherine Davis⁵, and Cara Kirby⁵

¹London Metropolitan University, London, UK, ²Imperial College, University of London, London, UK, ³St Helier Hospital, Carshalton, UK, ⁴Otsuka Europe Development and Commercialisation, Buckinghamshire, UK, and ⁵Hamell, London, UK

Correspondence to: Alison Carr; E-mail: alison@hamell.co.uk

Abstract

Background: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disorder; however, at the time this research was conducted, no disease-modifying treatment was currently available. Medical texts often describe early-stage disease (Stages 1 and 2) as asymptomatic, but there is evidence from patients of considerable physical and emotional effects.

Methods: In-depth interviews were conducted with 80 ADPKD patients, 72 nephrologists and 85 primary care physicians (PCPs) from nine European countries to explore the experience and impact of early-stage ADPKD. Interviews were transcribed, translated and analysed centrally using thematic analysis. An additional 600 physicians completed standardised online questionnaires to investigate perceptions of symptom severity and management of early-stage ADPKD.

Results: Eighty-eight per cent of patients with early-stage disease reported physical symptoms including pain, fatigue, breathlessness, weakness and a general malaise. However, 24% of nephrologists and 16% of PCPs perceived that the patients with early-stage disease did not experience any physical symptoms at all. There was a greater awareness of the emotional impact of disease, but this was still underestimated when compared with patient-reported experiences, which highlighted widespread feelings of loss, uncertainty and fear.

Patients and physicians experienced frustration due to the lack of treatment options, especially in the long latent period. For many patients, the inability to affect their disease course whilst living with a diagnosis resulted in feelings of hopelessness, helplessness and depression. Physicians identified a need for improved cooperation between health-care professionals, and increased psychological support for patients.

Conclusions: Early-stage ADPKD can have a significant physical and emotional impact on patients. Whilst some physicians have an awareness of patient experience during early-stage disease, most underestimate the impact of ADPKD. Both patients and physicians are negatively affected by their inability to alter disease progression.

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Key words: ADPKD, latent period, pain, psychology, quality of life

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disorder, affecting less than 5 in 10 000 people [1]. The disease is characterised by the development and progression of renal cysts, leading to increased kidney volume, reduced renal function and eventual progression to end-stage renal disease (ESRD) [2–4]. Initial clinical manifestations include haematuria, hypertension, pain, fatigue and gastrointestinal symptoms [3, 5].

In contrast to the severity of these latter stages, the early phase of ADPKD is often described as being asymptomatic, until the third or fourth decade of life when renal function begins to decline [6, 7]. No effective disease-modifying drugs are currently available to treat ADPKD; clinical management of early disease generally consists of hypertension control and disease monitoring [8, 9]. Limited research examining the initial phase of ADPKD prior to the development of chronic kidney disease (CKD) has been published; however, there is growing evidence to suggest that patients can suffer symptoms, such as pain and fatigue, during the early stage of their disease [10, 11]. Back pain is the most common factor leading to ADPKD diagnosis, often experienced by patients in early disease with normal renal function [10–13].

In addition to these physical symptoms, a diagnosis of ADPKD may have considerable psychological effects. In line with the other diseases that can be diagnosed years before the onset of pathognomonic symptoms, but for which no early treatment can be offered, the burden of knowledge of future disease may have negative psychological implications [14]. Even in those experiencing the classically described asymptomatic latent phase, the psychological impact of living with the disease remains [6]. Patients may live for many years with the knowledge of their diagnosis, aware that their disease is progressing but unable to take any action to ameliorate this process. Furthermore, due to its heritable nature, many patients will have witnessed the effects of ADPKD in close relatives and are conscious of the future that awaits them. These patients are, therefore, 'faced with an entity that affects their psychological and emotional state as well as their physical condition' [15]. Reductions in quality of life (QoL) and an increased rate of anxiety and depression are well described in CKD and ESRD patients, including those with late-stage ADPKD [15–17]. However, this research was directed towards the later stages of disease, and studies investigating the psychological well-being of pre-dialysis ADPKD patients are limited and inconclusive.

This study was undertaken to explore patient and physician experiences and perceptions of early-stage ADPKD.

Materials and methods

This cross-sectional study was designed to determine the experience and impact of ADPKD on patients in early-stage disease (CKD Stages 1 and 2) and to elicit the perceptions and beliefs of primary care physicians (PCPs) and nephrologists. All participants gave informed consent. Ethical approval was obtained from Reading Independent Ethics Committee (reference: 280613-1).

Subjects

Patients

A total of 80 patients over 18 years of age with a diagnosis of ADPKD were recruited through patient organisations and

advertisements in clinical centres. Patients were recruited from the following countries: 10 patients each from the UK, Germany, France, Italy and Spain (EU5 countries); 10 from both Finland and Denmark; and 5 from both Sweden and Norway.

Purposive recruitment was used to ensure that the distribution of patients in the sample group reflected all CKD stages of disease. Eleven per cent of patients had Stage 1 disease, 20% Stage 2, 19% Stage 3, 23% Stage 4 and 27% Stage 5. The mean age of participating patients was 50 years (SD 12.46, min–max 20–74 years), and 62% were female. Patients with early-stage disease provided information about their current level of symptoms and disease impact; those in later stages provided retrospective comments.

Physicians

From the same nine countries, 757 physicians were recruited from online communities and panels of doctors expressing a willingness to participate in the research. Of these, 157 participated in interviews, of which 72 were nephrologists and 85 were PCPs. A further 300 nephrologists and 300 PCPs completed online questionnaires. The number sampled from each country reflected the distribution of PCPs and nephrologists across Europe.

Eligible physicians were over 25, qualified and practising within their specialty for over 1 year, with at least 50% of their time in direct patient care. Nephrologists managed three or more ADPKD patients per month, and PCPs at least two patients every 6 months.

Data collection and analysis

Subjects took part in one-to-one semi-structured telephone interviews of ~1 h conducted by trained qualitative interviewers. Interview questions were designed by clinical experts and qualitative researchers to allow a full exploration of the areas of interest. Patient topics included their disease and treatment pathway; understanding of and reaction to their diagnosis; and experiences, understanding, perceptions, beliefs and expectations of ADPKD and its treatment. Physician topics included assessment of severity and stage of ADPKD; perceptions of the impact of early disease on patients; and their awareness, experience and role in the management of early-stage disease. All interviews were recorded, transcribed and translated into English. Using a phenomenological approach, each transcript was thematically analysed by two qualitative researchers. Commenting and coding were performed to allow interpretation as well as categorisation of the data. Codes were compared and, in cases of disagreement, codes were agreed following discussion. Analysts worked together to develop and agree themes.

Interview responses were used to construct standardised questionnaires capturing physician perceptions of the impact of early-stage ADPKD. A further 600 participants completed these online, and descriptive statistics were used to analyse data from the quantitative questionnaire data using SPSS v19.

Results

Current experiences of patients with early-stage disease

Physical symptoms in early-stage ADPKD

Considerable physical symptoms of early-stage disease were reported in this study by patients with early-stage disease. Of the 25 patients currently with CKD Stage 1 or 2, 22 (88%) reported

symptoms including back, abdominal or kidney pain, fatigue, breathlessness, weakness and general malaise (Table 1). In most patients, these symptoms were severe enough to inhibit work and physical activity/exercise.

Theme 1: Pain and discomfort. Patients in early-stage disease described both intermittent pain—with acute episodes of severe pain (for example, when a cyst ruptured)—and more prolonged episodes of poorly defined backache or a feeling of abdominal heaviness. Discomfort or breathlessness caused by abdominal bloating and a feeling of pressure was commonly reported. For some patients, discomfort was related to repeated urinary tract infections or digestive problems.

Table 1. Patient experiences of physical symptoms in early-stage ADPKD

- Tiredness and fatigue
- Pain and discomfort

Illustrative quotes from patients with early-stage ADPKD:

‘In hindsight, the problems that I’ve had and just assumed that’s how I am, are symptoms that I’ve suffered with and I’d never connected the dots. But I’ve different problems with back ache and aching and gastrointestinal problems. So all these things I’d got but I’d never had a formal diagnosis for something that caused all those symptoms.’ [UK 053]

‘The pain was unbearable at certain times.’ [DE 218]

‘It’s not back pain, it’s not in the bones or joints, it’s not in the muscles. But sometimes I have a strange feeling in my back, there where the kidney is.’ [FI 002]

‘I don’t have that much strength any more.’ [DE 218]

‘You are always tired, you are breathless after a walk.’ [FN 10103]

Theme 2: Fatigue and weakness. Although fatigue and weakness were more severe and more frequently reported in later-stage disease, some patients were significantly inhibited by these symptoms pre-diagnosis, or in early disease.

Emotional impact of diagnosis

During early-stage disease, the psychological impact of ADPKD was widespread and represented by the three main themes described below. For many patients, the emotional impact of the diagnosis was devastating, either because they had witnessed the effects of ADPKD in a close relative, or in sporadic cases due to the unexpected nature of the diagnosis (Table 2).

Theme 1: Loss. Many patients described early disease as a time of loss. For patients with a family history, the diagnosis confirmed their fears, and they described a time of grieving for the loss of the lives they had hoped to live. Patients described loss in relation to having children, life expectancy, living a healthy life and valued activities.

Theme 2: Uncertainty. Patients described frustration and anxiety caused by uncertainty about the progression of their disease. They were caught in the unsettling situation of being certain about the outcome of their disease, but uncertain about the timing and rapidity of progression. Some patients felt that this was compounded by a lack of definitive information from their physicians.

Theme 3: Fear. Most patients described fear for themselves or their children for the course and outcome of the disease. This fear was often exacerbated by uncertainty and was associated with feelings of emotional distress including anxiety and depression.

Patient experience of the latent period

Further analysis of patient interviews revealed four themes providing insight into the experiences and frustrations of living with

Table 2. Patient experience of ADPKD diagnosis and latent period

ADPKD diagnosis

- Loss
- Uncertainty
- Fear

Latent period

- Long latent period with no treatment and little contact with health-care professionals
- Hopelessness and helplessness
- Distress and frustration
- Coping strategies

Illustrative quotes:

Diagnosis:

‘The word “fatal” was used a lot.’ [UK 053]

‘It’s a bit unsure when you don’t know how fast this disease will advance. You are always thinking when will it be the stage where dialysis is needed.’ [FI 001]

‘Afraid of the future. There are people who think that something bad could or couldn’t happen. I already know that something bad will happen for sure.’ [IT 900]

‘Honestly I am scared now. As much as I did not care before, now I am scared.’ [FR 311]

Latent period:

‘In my case they couldn’t do so much—it took 20 years before we began with the treatments.’ [FN 10101]

‘It took about 12–13 years. The kidneys functioned quite well. I went for frequent follow-ups so as long as they function well you do not do anything. At least not at that point.’ [SWE 10008]

‘I wish I hadn’t known about it because it was like living with a ticking time bomb.’ [UK 098]

‘I am just waiting for when it will get worse. It is just waiting.’ [FI 001]

‘When it comes to treatment they have not told me much, because they do not know much themselves.’ [NOR 10203]

‘I maintain my weight, I don’t drink excessively, I don’t smoke, I try and have a low salt diet, I try and have a healthy diet. . . . I think all of those things are worth doing.’ [UK 107]

‘Then I mainly tried to forget about the disease.’ [FI 001]

ADPKD during the latent phase, when the diagnosis has been made but treatment is not available (Table 2). All patients were included in the analysis for Theme 1, to allow representation of the entire latent period. Only interviews from patients in the early stages were examined for Themes 2–4.

Theme 1: Management during early stages. Some patients described latent periods of up to 40 years. Management during this phase included regular but infrequent visits to their physician, with some patients reporting intervals of over a year. Blood pressure monitoring and management of hypertension were the main intervention during this phase.

Theme 2: Hopelessness/helplessness. Fifty-six per cent of early-stage patients reported feelings of hopelessness and helplessness during the latent period. Patients described inevitable disease progression, with their condition advancing towards an unavoidable end point with no possibility of improvement or cure. This inability to influence their disease often led to frustration, with some expressing feelings of anxiety and depression.

Theme 3: Distress and frustration associated with their care. Some patients experienced considerable distress and frustration associated with their care during the latent period. This often resulted from the fact that their physicians were unable to offer disease-modifying treatment. Many patients found the information supplied by their health-care professionals inadequate and some reported that physicians lacked sufficient knowledge relating to ADPKD. For some patients, this was compounded by physicians underestimating the severity of their symptoms.

Theme 4: Coping strategies for the latent period. Despite the negative impact of ADPKD diagnosis on the majority of patients, some reported coping strategies to aid them in the pre-symptomatic stage. These generally fell into one of two categories: lifestyle modification, to improve overall health; or denial—several patients described trying to forget about their diagnosis, or that they considered their disease as something imaginary and they should ‘get on with my life’.

Physician perceptions and experiences

Perception of the patient experience

The frequency of physical effects reported by patients was not reflected in physician perceptions of the disease. Overall, 24% of nephrologists and 16% of PCPs thought that patients with early-stage ADPKD did not experience any physical symptoms. Sixty-seven per cent of nephrologists and 65% of PCPs believed that patients experienced only mild physical symptoms, and 78% of nephrologists and 62% of PCPs thought that early-stage ADPKD had no impact on daily activities (Table 3). There was a greater awareness of the emotional impact of early-stage disease amongst physicians, but this was still underestimated when compared with patient self-reported experiences. Overall, 5% of nephrologists and 7% of PCPs believed that early-stage disease has no emotional impact on patients, and 47% of nephrologists and 45% of PCPs thought that the emotional impact was mild (Table 4).

Physician experiences

Several themes were revealed regarding the management of patients with early-stage ADPKD (Table 5).

The majority of physicians viewed their role during early-stage ADPKD as symptom management, and provision of

Table 3. Nephrologists' and PCPs' perceptions of the severity of physical symptoms experienced by patients during early-stage ADPKD

| | Nephrologists N (%) | PCPs N (%) |
|----------|------------------------|---------------|
| None | 73 (24.3) | 48 (16.0) |
| Mild | 201 (66.8) | 196 (65.3) |
| Moderate | 26 (8.6) | 54 (18.0) |
| Severe | 1 (0.3) | 2 (0.7) |
| Total | 301 (100) | 300 (100) |

Responses from the additional physicians who completed the online questionnaire.

Table 4. Nephrologists' and PCPs' perceptions of the severity of the emotional impact on patients of early-stage ADPKD

| | Nephrologists N (%) | PCPs N (%) |
|----------|------------------------|---------------|
| None | 15 (5.0) | 21 (7.0) |
| Mild | 141 (46.8) | 135 (45.2) |
| Moderate | 120 (39.9) | 129 (43.1) |
| Severe | 25 (8.3) | 14 (4.7) |
| Total | 301 (100) | 299 (100) |

Responses from the additional physicians who completed the online questionnaire.

information and psychological support. Many participants stressed the importance of education and information, with some suggesting that this area is neglected. During the latent period, close monitoring and management of blood pressure were considered critical.

Both PCPs and nephrologists reported a strong desire for treatment to offer their patients early in the course of disease. Many considered that increased psychological support during the latent period and increased cooperation between PCPs and nephrologists would be beneficial. Many physicians expressed frustration, the main contributing factors being inevitable disease progression and the lack of treatment options. Some physicians were frustrated by the medical system, desiring earlier specialist referral and access to additional support for patients, for example, from psychologists.

Reflecting the opinion of some patients, many PCPs expressed their lack of knowledge of the disease, which led to discomfort when dealing with ADPKD patients. Additional training courses or educational material on the subject was mentioned. Furthermore, negative language was frequently used by PCPs when referring to ADPKD as a condition, the QoL of patients and the experience of diagnosing the disease.

Discussion

This study assessed the experience, management, perceptions and expectations of ADPKD during diagnosis and the latent phase both in patients and physicians. Despite the accepted description that early disease is largely asymptomatic, patients experience considerable physical symptoms and negative emotional effects during early-stage disease. Physicians particularly underestimate the physical symptoms.

Our findings show that physical symptoms attributed to ADPKD were widely reported by patients with early disease and

Table 5. Physician experience of ADPKD

Shared themes:

- 'Role perception: View of their role during latent period
- 'Desire for early support: Desired improvements to service/treatments offered during early disease
- 'Treatment frustrations: Frustration as a result of the lack of treatment available, and with the medical system during the long latent period

PCP specific themes:

- 'Lack of treatment knowledge and confidence: PCPs lack the knowledge and confidence to treat patients, preferring to refer early to a nephrologist
- Negative ADPKD language: PCPs use negative language when talking about ADPKD

Nephrologist themes:

- Need for psychological support: Nephrologists feel that increased psychological support for patients would be beneficial

Illustrative quotes:

PCP:

'To inform them about their condition and advise them on diet and exercise, risks with this condition. And I would monitor them, and refer them if I felt this was required.' [NOR 08]

'These people are often very scared, so that they become psychologically disabled. Mental support is important at the early stage cases.' [FIN 01]

'If there was a therapy that treats the cause of ADPKD and prevents the progression, I would use it instantly after diagnosis.' [GER 05]

'It feels quite frustrating, not having a treatment that is able to reduce the symptoms in the long term for the patients.' [SWE 05]

'Feeling of not knowing and a lot of insecurity: I wouldn't know how to manage it.' [SP 09]

'A really bad, bad disease to get', 'it's awful for the diagnosed patient', 'regrettable and severe disease', 'a disease which can't be cured, and a diagnosis which is very difficult to announce to patients.' [DEN 03, FIN 01, 03, FRA 03]

Nephrologist:

'The most important thing I can do is to inform them about the disease.' [SWE 06]

'Blood pressure, blood pressure, blood pressure. . . and blood pressure one more time.' [DEN 08]

'The only imaginable therapy that could improve these patients' life would be a treatment which slows down the growth of cysts.' [ITA 08]

'I would say that it is the psychological support that is most important.' [FRA 02]

'(the diagnosis). . . it can be a brutal shock.' [FRA 03]

' . . . there might also be a psychologist so that he prepares the patient for the future.' [SP 01]

were often severe enough to inhibit daily activities. In this study, most physicians acknowledged that patients with early-stage disease may experience physical symptoms including pain, but describe these as uncommon. It has previously been suggested that pain is frequently under-reported by ADPKD patients [18] and under-recognised by physicians, leading to inadequate pain management, particularly in the early stages of disease [19, 20]. Our study supports this finding, highlighting a discrepancy between the physical symptoms reported by patients and the perception by physicians that many patients are asymptomatic. To avoid recall bias, this analysis focussed on patients currently experiencing early-stage disease. However, the results were supported by retrospective comments made by patients in later stages.

Physicians seemed more likely to accept the likelihood of physical symptoms in early disease when there was a medical explanation such as a burst cyst, whereas they struggled to attribute pain to ADPKD where there was no explanation that fit their medical model. However, previous research has shown that both renal and extra-renal abnormalities are present in ADPKD far in advance of impaired renal function, with early detection of cysts and increased total kidney volume along with disruption of many other parameters [6, 7, 21]. The early presence of these manifestations provides an explanation for patients' experience of pain, suggesting that greater attention should be paid to symptoms in the period preceding declining renal function. Physicians were much more aware of the emotional and psychological impacts of early-stage disease, although they probably still underestimate the far-reaching impact it has on patients' QoL and well-being.

There has been increasing interest in the psychological effects of many medical conditions, including renal disorders such as ADPKD [15]. In general, many authors conclude that psychological disorders such as anxiety and depression are likely to be under-diagnosed, underestimated and certainly under-treated

in patients with CKD, including those with ADPKD [10, 17, 22–24]. However, research examining the earlier stages of ADPKD has been limited and shown conflicting results [16, 17, 25]. This study explored the psychological impact of living with ADPKD during the latent period of disease, indicating that ADPKD patients can suffer considerable psychological difficulties as a result of their diagnosis for years prior to the onset of CKD. In general, patients felt that they were waiting for their disease to progress, leading to considerable distress, frustration and associated negative effects such as depression in some.

Taken together, these findings suggest a lengthy period during which some patients are suffering from pain and fatigue, and many patients are experiencing psychological distress, but physicians are unaware of or underestimating their difficulties. These results challenge the currently accepted description of early-stage disease as asymptomatic and suggest that increased access to pain management and psychological support would likely improve management within the current framework of care.

This study is the first to assess the impact of the latent period on physicians as well as patients. Both PCPs and nephrologists expressed frustration at the lack of disease-modifying treatments available (at the time this research was conducted) and their subsequent inability to hinder disease progression. Some PCPs felt uncomfortable with their lack of knowledge and inexperience in dealing with ADPKD, mirroring the feelings expressed in patient interviews. In contrast, nephrologists generally appeared confident in these areas, despite some patients expressing dissatisfaction regarding these aspects of their specialist care. Physicians from both the groups felt that increased psychological support for patients in the early stages of the disease may be beneficial.

The use of qualitative analysis relies on smaller sample sizes than quantitative studies. Analysis of the large amounts of

interview data produced is a subjective process; however, this is performed by trained researchers using well-established methods to interpret the wealth of information produced. Qualitative methodologies offer the opportunity to allow in-depth exploration and insight into experiences, attitudes and beliefs. As such, objective measures of a single aspect of disease (such as pain) would result in a narrower picture of ADPKD, and a qualitative, interview-based approach was considered appropriate for this study. This research advances the understanding of the impact of ADPKD on patients and physicians across nine European countries. Further research would be useful to explore cultural differences in patient experience and physician perceptions.

In conclusion, this study demonstrates the negative physical and emotional effects of ADPKD from the time of diagnosis throughout the latent period. Whilst some physicians have an accurate awareness of patient experience during early-stage disease, most underestimate the impact of ADPKD. These results highlight the frustration experienced by patients and physicians at their inability to affect disease outcome. Nonetheless, in the absence of active treatment options, suggestions can be made to improve patient and physician experiences of this disease.

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Conflicts of interest statement

A.M. is an employee of Otsuka. The research was sponsored by Otsuka. Hamell was paid by Otsuka to design and implement the research and to analyse the data. Otsuka had no access to the raw data, and the analysis was conducted completely independently by Hamell.

The results presented in this paper have not been presented previously in whole or part except in abstract form.

Authors' contributions

A.C. designed and performed the research and wrote and reviewed the paper. C.D. and C.K. performed the research and reviewed the paper. A.M. was involved in the study design and reviewed the paper. J.M. was involved in the study design, reviewed the data and wrote and reviewed the paper. D.K. and A.B. reviewed the data and contributed to and reviewed the paper. Hamell undertook the analysis.

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