EPH95

Claims data analysis of the prevalence and healthcare resource utilization of chronic kidney disease-associated pruritus in German hemodialysis patients

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Background

- Significant numbers of patients with chronic kidney disease (CKD) on hemodialysis (HD) experience severe pruritus and/or dry skin, referred to as chronic kidney disease-associated pruritus (CKD-aP).
- In Germany, the prevalence of CKD patients on HD suffering from moderate to extreme itching was estimated to be 27.0% based on register data.[1]
- Past studies in Germany mostly used individual questionnaires to regionally assess the prevalence of CKD-aP
- Due to the subjective nature of pruritus and the reliance on patient self-reporting, which introduces a degree of variability and potential inaccuracies into the diagnostic process, the diagnosis and treatment of CKD-aP is challenging.

Objectives

- To assess the prevalence of patients with CKD-aP
- To compare clinical characteristics in CKD patients on HD with and without CKD-aP

Methods

Study design & Data source

- Administrative claims data of the Statutory Health Insurance (SHI) in Germany provided by the Institute for Applied Health Research Berlin (InGef) was used for this study.
- The database comprises an adjusted anonymized data set of about four million SHI-insured persons, which corresponds to 4.8% of the German population.[2]
- The database is representative for the German population in terms of age and sex and has been shown to reflect well the morbidity, mortality, and drug use of the general German population.

Study timeframe and population

- In a timeframe of six years (2014-2019), adult CKD patients with long-term HD were selected.
- CKD was identified via ICD-10-GM codes and HD with “Uniform assessment standard” (EBM) or “Key of operations and procedures” (OPS) codes.
- Stratification of the patients was performed based on the presence or absence of ICD-10-GM codes (L28.-, L29.-, L98.1 and F45.8) as proxies for CKD-aP.
- To ensure the long-term character of HD, only patients with at least three HD sessions in each of eight successive quarters were included.
- Exclusively patients above 18 years and no evidence of a kidney transplantation within the study’s timeframe were selected.
- Regarding age and sex, the two groups were statistically comparable as measured by the standardized mean difference (SMD) to a level of 0.1, obviating the need for a further matching of the two comparison groups.

Study outcomes

- Comorbidities were assessed by ICD-10-GM codes and compared related to their prevalence using Chi-square test or Fisher`s exact test.
- In addition, in both groups, the relative risk (RR), risk differences (RD), and odds ratio (OR) were calculated for the comorbidities.

Results

Patient population

- A total of 4,352 CKD patients with long-term HD were identified.
- From these 273 patients with CKD-aP and 3,076 patients without a pruritus diagnosis were identified.
- CKD-aP patients represent 6.3% of all CKD patients on long-term HD.
- Of the patients with CKD-aP, 240 (87.9%) had a diagnosis of L29.-, 50 (18.3%) had a diagnosis of L28.-, 34 (12.5%) had a diagnosis of F45.8 and <5 (<1.8%) had a diagnosis of L98.1. (Percentages do not sum up to 100% as patients could have various diagnosis codes)
- The mean age of the CKD-aP patients was 75 years, while that of the patients without CKD-aP was 74 years. Slightly more males were represented in both groups (55.7% and 60.3%).

Table 1: Patient characteristics

Patient characteristics		HD CKD patients with CKD-aP (N=273)		HD CKD patients without CKD-aP (N=3,076)		Statistical parameters
		n, mean	%	n, mean	%	SMD
Gender (male)		152	55.7	1,855	60.3	0.09
Age, mean (SD)		75 (11.1)		74 (12.4)		0.08
Age, by age groups (years)	18-65	49	18.0	664	21.6	0.09
	66-75	64	23.4	676	22.0	0.03
	76-85	113	41.4	1,237	40.2	0.02
	≥86	47	17.2	499	16.2	0.03
Number of dialysis sessions mean (SD)*		153.2 (24.3)		151.4 (22.3)		0.08

*In the outcome assessment period of 12 months.

Comorbidities

- The prevalence of each comorbidity and the ORs that were calculated and used as the basis for presenting the comorbidome are shown in Table 2.

Table 2: Selected comorbidities

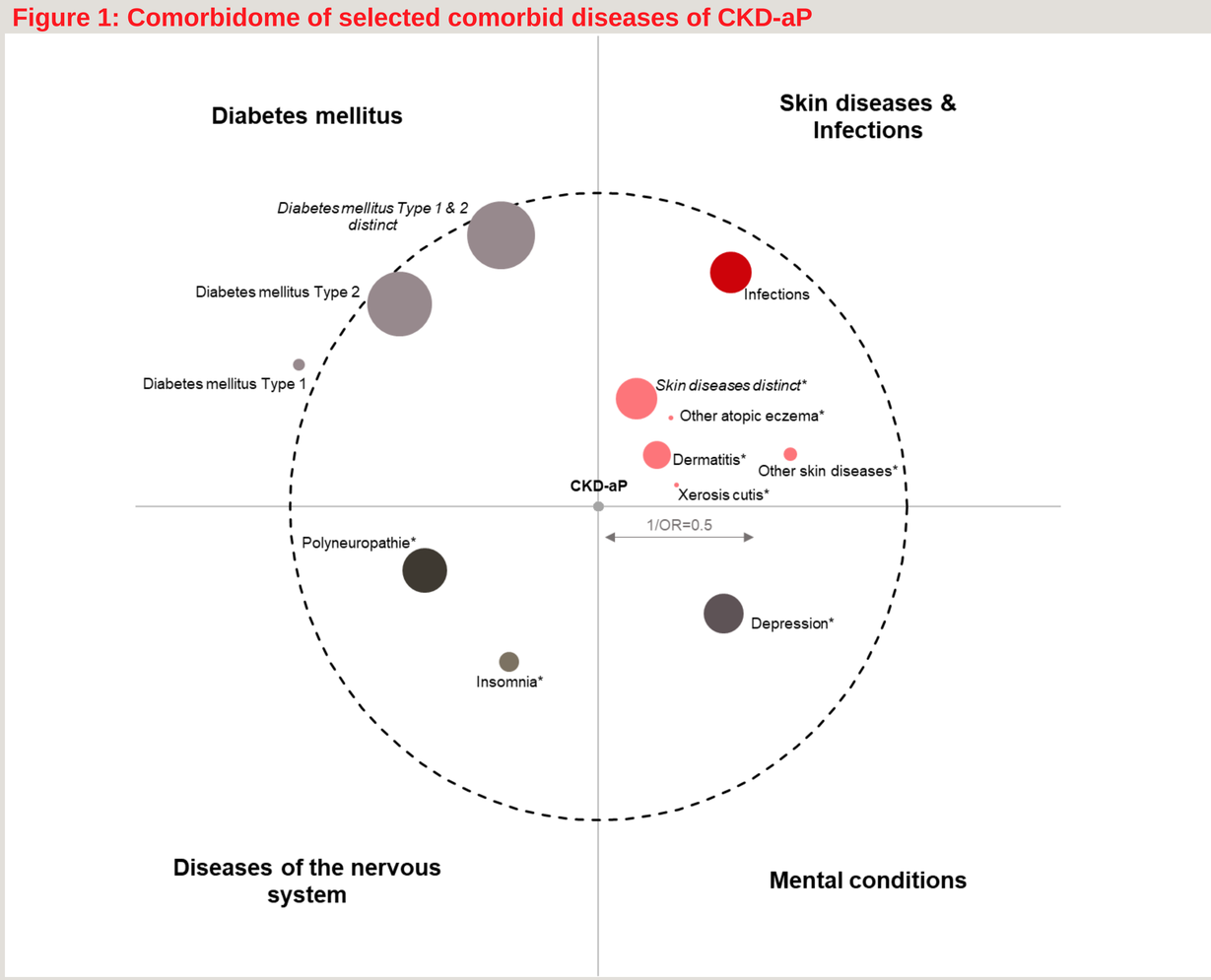
Comorbidities	HD CKD patients with CKD-aP (N=273)		HD CKD patients without CKD-aP (N=3,076)		Statistical parameters	
	n	%	n	%	OR	p-value
Other atopic eczema	12	4.4	51	1.7	2.7	**0.0014**
Dermatitis	65	23.8	224	7.3	4.0	**<0.0001**
Other skin diseases	32	11.7	243	7.9	1.6	**0.0275**
Xerosis cutis	12	4.4	37	1.2	3.8	**0.0004**
Distinct[1]	*94*	*34.4*	*493*	*16.0*	*2.8*	***<0.0001***
Diabetes Type 1	26	9.5	312	10.1	0.9	0.7448
Diabetes Type 2	149	54.6	1,606	52.2	1.1	0.4527
Distinct[2]	*154*	*56.4*	*1,669*	*54.3*	*1.1*	*0.4939*
Depression	91	33.3	647	21.0	1.9	**<0.0001**
Insomnia	47	17.2	329	10.7	1.7	**0.0011**
Infections	95	34.8	969	31.5	1.2	0.2622
Polyneuropathy	104	38.1	828	26.9	1.7	**0.0001**

The following ICD-10-GM were used to identify the respective comorbidities:
Other atopic eczema (L20.8, L20.9), Dermatitis (L30.0, L30.1, L30.3, L30.4, L30.8, L30.9), Other skin diseases (L98.4, L98.8, L98.9), Xerosis cutis (L85.3), Distinct[1] (L20.8, L20.9, L30.0, L30.1, L30.3, L30.4, L30.8, L30.9, L98.4, L98.8, L98.9, L85.3), Diabetes Type 1 (E10.-), Diabetes Type 2 (E11.-), Distinct[2] (E10.-, E11.-, E13.-, E14.-), Depression (F32.0, F32.1, F32.2, F32.8, F32.9, F33.0, F33.1, F33.2, F33.4, F33.8, F33.9), Insomnia (G47.0, G47.2, G47.8, G47.9), Infections (A09.0, A49.9, B99, B96.2, Z11, T82.7), Polyneuropathy (G63.2, G63.3, G63.8)

- We used a comorbidome to graphically represent the prevalence of comorbidities and their correlation with the risk of a CKD-aP diagnosis (see Figure 1). Bubble areas represent the respective comorbidity prevalence. Their proximity to center indicates strength of correlation with CKD-aP diagnosis risk. Scaling is based on 1/OR. Bubbles inside dotted orbit increase CKD-aP diagnosis risk (1/OR<1), outside decrease it (1/OR>1).
- Comorbidities presented reflect diseases that are commonly mentioned in the literature as often occurring in CKD-aP patients and thus affecting the patients' quality of life[3,4,5]. Comorbidities such as dermatitis (OR=4.0), depression (OR=1.9), insomnia (OR=1.7) and polyneuropathy (OR=1.7) were significantly more common in patients with CKD-aP.

Results (Continued)

Figure 1: Comorbidome of selected comorbid diseases of CKD-aP



* refers to significant differences in the prevalence between both patient groups based on chi square or Fisher’s exact test, respectively. A p-value of <0.05 was considered as statistically significant.

Pharmaceutical treatment

- Substantial disparities were observed in the prescription patterns of various medications between patients diagnosed with CKD-aP and those without.
- This included antihistamines (prescribed to 36.3% of CKD-aP patients vs. 7.7% of non-CKD-aP patients, p<0.01), topical corticosteroids (27.8% vs. 5.6%, p<0.01), pharmacy compounded mixtures (22.3% vs. 4.7%, p<0.01), gabapentin and pregabalin (29.3% vs. 16.3%, p<0.01), as well as opioids (43.6% vs. 33.5%, p<0.01).
- Among opioids, tramadol and hydromorphone were most commonly prescribed, with significant differences between patients with and without CKD-aP, resulting in prescription rates of 10.3% vs. 6.3% (p=0.01) and 8.1% vs. 4.8% (p=0.02), respectively.

Table 3: Selected pharmaceuticals

Pharmaceuticals	HD CKD patients with CKD-aP (N=273)		HD CKD patients without CKD-aP (N=3,076)		Statistical parameters	
	n	%	n	%	OR	p-value
Non-sedative antihistamines	46	16.9	79	2.6	7.7	**<0.0001**
Sedative antihistamines	65	23.8	170	5.5	5.3	**<0.0001**
Distinct	*99*	*36.3*	*238*	*7.7*	*6.8*	***<0.0001***
Anti-anxiolytics	38	13.9	219	7.1	2.1	**0.0001**
Sedatives	37	13.6	351	11.4	1.2	0.2892
Distinct	*70*	*25.6*	*526*	*17.1*	*1.7*	***0.0004***
Gabapentin	51	18.7	245	8.0	2.7	**<0.0001**
Pregabalin	35	12.8	277	9.0	1.5	**0.0377**
Distinct	*80*	*29.3*	*502*	*16.3*	*2.1*	***<0.0001***
Opioids	119	43.6	1,030	33.5	1.5	**0.0008**
Topical corticosteroids	76	27.8	171	5.6	6.6	**<0.0001**
Pharmacy compounded (topical) mixture	61	22.3	143	4.7	5.9	**<0.0001**

Discussion

- Since a variety of ICD-10-GM codes are applicable for the diagnosis of CKD-aP, the actual coding practice of physicians for pruritus is unknown.
- Further, some physicians may not be aware of CKD-aP as a distinct condition or may be unsatisfied with the lack of ICD-10-GM codes and instead use dermatologic codes to document a patient's symptoms.
- Around a third of patients were prescribed sedative and non-sedative antihistamines, and topical creams. Antihistamines are commonly used for pruritus treatment, but their efficacy varies.
- In Germany, Burton et al. found that 48%/41% of nephrologists commonly used oral/topical antihistamines and 36% used topical corticosteroids.[6] However, some antihistamines have contraindications or require dosage adjustments for CKD or HD patients. The S2k-guideline doesn’t recommend antihistamines for nephrogenic pruritus patients.[7]
- The significant co-occurrence of skin diseases and the frequent use of opioids, particularly traditional opioids (mu opioid receptor agonists) which can increase itchiness as a side effect despite alleviating pain, highlight the diagnostic complexity of CKD-aP.
- Given this complexity, it is recommended that further analysis be performed to gain a more comprehensive understanding of the diagnostic process.

Conclusions

- The comparatively low and likely underestimated prevalence, consisting of 6.3% of all CKD patients with long-term HD having CKD-aP, underscores the importance of a unique ICD code for CKD-aP in the new ICD-11 catalog.
- In addition, CKD-aP has been shown to be associated with a high incidence of depression and infection, underscoring the increased existing disease burden.

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Disclosures

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