

Facharztpraxis Nephrologie
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Table 1. The number of patients per group and their gender, classified according to their CKD stage

CKD stage	Number of patients (male/female)			Total
	Average age	With HZ	Without HZ	
1–3	73.78	0/2	38/41	81
4 and 5	74.21	3/1	22/13	39
5D (ESRD)	72.89	4/4	26/21	55
		7/7	86/75	175

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End-stage renal disease (ESRD) contributes to the increasing prevalence of herpes zoster

Sir,
Varicella-zoster virus (VZV) causes two clinically distinct diseases: varicella (chickenpox) and herpes zoster (HZ; shingles). The lifetime cumulative incidence is ~10–20% of the population [1]. The incidence rates progressively increase with age, presumably owing to decline in the VZV-specific cell-mediated immunity [2]. Age is the most important risk factor for the development of HZ; however, immunocompromised patients such as transplant recipients, patients receiving selective immunomodulatory therapy and HIV-infected patients have an increased risk of VZV reactivation [3,4]. Further, immunosuppressed individuals with HZ exhibit a significantly higher rate of complications (e.g. dissemination of the disease and ocular involvement) [5].

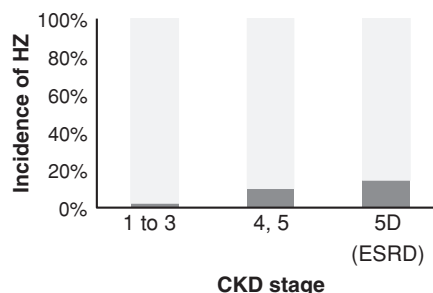


Fig. 1. The graph shows the incidence (%) of HZ in patients classified by chronic kidney disease (CKD) stage.

Patients who have end-stage renal disease (ESRD) with uraemia exhibit an impaired host immune response. The reported immunological abnormalities in ESRD patients include decreased phagocytic function of granulocytes and monocytes/macrophages, defective antigen presentation by monocytes/macrophages, reduced antibody production by B lymphocytes and impaired T-cell-mediated immunity [6]. Physicians working in dialysis facilities generally presume that ESRD contributes to the increase in the prevalence of HZ. Despite this presumption, the morbidity of HZ in ESRD has not been previously reported.

This retrospective study includes information on all septuagenarian patients who visited the outpatient clinic of the nephrology division and dialysis centre affiliated to our university. A total of 220 patients were followed up for at least 3 years within the last 3.5 years. Of these 220 patients, 45 were excluded from this study because they exhibited one or more already identified risk factors for HZ (e.g. corticosteroid and/or immunomodulatory therapies, carcinomas and autoimmune disorders). Potential patients were identified by searching the diagnostic and billing codes of hospital records. If HZ was confirmed in a patient, the medical records were reviewed to verify that the case of HZ was indeed a new one. Our results revealed that the incidence of HZ increased with the progression in the stages of chronic kidney disease (CKD) (Table 1, Figure 1). In fact, the incidence rate of HZ was 84.8 per 1000 person-years in our outpatients undergoing haemodialysis or continuous ambulatory peritoneal dialysis. However, in patients with CKD stage 1, 2 or 3, the incidence rate (8.2 per 1000 person-years) was as low as that in septuagenarian HZ patients without kidney disease [5]. Diabetic nephropathy is the most important cause of ESRD that requires renal replacement therapy. Diabetes as well as CKD is a risk factor for some infectious diseases because these conditions result in a compromised immune system. However, the incidence of HZ and diabetes was not found to be significantly

related as determined by the examinations performed in our hospital followed by analysis with the chi-square test.

We concluded that ESRD, which requires renal replacement therapy, may contribute to the increased prevalence of HZ.

Conflict of interest statement. None declared.

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Hydrochlorothiazide-induced tubulointerstitial nephritis in a patient with Dent disease

Sir,

Dent disease is an X-linked renal tubular disorder characterized by low-molecular-weight proteinuria and combinations of hypercalciuria, nephrolithiasis, nephrocalcinosis and aminoaciduria. Some have progressive renal failure. It is caused by mutations in *CLCN5* gene encoding chloride/proton exchanger CLC-5 [1]. Nephrolithiasis and nephrocalcinosis increase risk of loss of renal function [2]. Hypercalciuria is a risk factor for stone formation. Thiazide diuretics reduce hypercalciuria and are recommended for treatment of Dent disease [3]. We describe acute renal failure (ARF) in a patient with Dent disease treated with hydrochlorothiazide.

Dent disease was diagnosed in a 12-year-old boy with rickets, short stature, renal insufficiency, hypophosphataemia, hypercalciuria, aminoaciduria, proteinuria and increased β_2 -microglobulin excretion. *CLCN5* gene sequence analysis showed a G→C nucleotide substitution in exon 9 of the *CLCN5* gene. He was treated with angiotensin-converting enzyme inhibitor to reduce proteinuria and preserve renal function. This was complicated by increase in serum creatinine (sCr) and discontinued. For hypercalciuria, he was treated with hydrochlorothiazide (0.5 mg/kg/day) and citrate. At that time he was 13 years old, with sCr 1.4 mg/dl and estimated glomerular filtration rate 72 ml/min/1.73 m² (Figure 1). Eleven weeks later he was asymptomatic without fever, rash, arthralgia or oliguria. Physical examination, hydration and blood pressure were normal. sCr was 11.1 mg/dl, phosphorus 9.4 mg/dl, uric acid 9.7 mg/dl, potassium 4.0 mmol/l, bicarbonate 26 mmol/l and haemoglobin 9.8 g/dl. White blood cell (WBC) count was 9600/cm² with 4.1% eosinophils (count 394). Urinalysis showed one plus protein, 10–25 WBCs and negative stain for eosinophils. Renal ultrasound showed 0.3 cm stone in the upper pole of the left kidney, without renal oedema or enlargement. There was no history of drug allergies or use of nephrotoxic medications. Presumptive diagnosis was tubular interstitial nephritis (TIN) induced by hydrochlorothiazide, which was then discontinued. sCr decreased only to 10.1 mg/dl in the next 2 days, and therefore he was treated with methylprednisolone (10 mg/kg/dose) for 3 days followed by oral prednisone, 60 mg/day, for 5 days. sCr was 4.9 mg/dl at the start of corticosteroid taper. This resulted in near-complete restoration of renal function (sCr 2.3 mg/dl) (Figure 1). Therefore, a renal biopsy was not done.

Renal complications of thiazide diuretics are acute TIN and ARF, typically developing 4–10 weeks after starting therapy. Withdrawal of the medication, with or without corticosteroids, restored renal function in reported cases [4]. Thiazides are classified as sulfonamides, which can cause hypersensitivity reactions, such as acute TIN. Renal biopsies of patients with ARF associated with thiazides show acute TIN without immune complex or anti-tubular basement membrane antibody deposits [4]. The report on use of hydrochlorothiazide in children with Dent disease described muscle cramps, hypovolaemia, hypokalaemia and hyponatraemia [5]. Our patient developed ARF as a complication of treatment of hypercalciuria with a thiazide diuretic. This should be kept in mind when prescribing thiazide diuretic to these patients.

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