

Drug-related problems in pediatric patients with chronic kidney disease: A single-center prospective study

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Abstract. Currently, there is a lack of data on drug-related problems (DRPs) in pediatric patients with chronic kidney disease (CKD) in China. The aim of the present study was to determine the incidence and determinants of DRPs in pediatric patients with CKD and to inform evidence-based pharmacotherapy for this population. For this purpose, a single-center prospective study was conducted at the Guiyang Maternal and Child Health Care Hospital (Guiyang, China) between January and December 2023. The Pharmaceutical Care Network Europe (PCNE) taxonomy [version 9.1 (v9.1)] was adapted to reflect the unique characteristics of pediatric patients with CKD; all identified DRPs were classified according to the modified PCNE v9.1 and were subsequently analyzed. The results demonstrated that among the 383 hospitalized children with CKD, 136 patients (35.51%) experienced 203 DRPs; the majority of problems pertained to treatment effectiveness (190; 93.60%) and of the 223 underlying causes identified, 79 (35.43%) were related to drug selection. Clinical pharmacists initiated 254 interventions; 243 (95.67%) were fully accepted and implemented. In conclusion, the present study demonstrated that DRPs are common in pediatric patients with CKD. The implementation of a pharmacist-led medication reconciliation model, supported by an adapted PCNE tool, was associated with a high intervention acceptance rate. However,

the present study was conducted in a single center and the findings obtained need to be validated in other centers, thereby providing more valuable references for the identification and management of DRPs in children with CKD.

Introduction

Medication reconciliation (MR) is defined as the systematic process of comparing a current medication regimen of a patient with prescribed orders to ensure consistency (1,2). Through MR, clinical pharmacists can identify actual or potential drug-related problems (DRPs), supervise and intervene in the medication-taking behaviors of patients, and promptly negotiate and adjust therapeutic plans with the multidisciplinary team to safeguard the safety and efficacy of pharmacotherapy. Over the years, the incidence of DRPs has been gradually increasing among various diseases and populations, leading to adverse effects on the therapeutic outcomes of diseases and individual health. For example, Venugopal *et al* (3) conducted a systematic analysis of 11 prospective studies and six retrospective studies, and revealed that the incidence of DRPs in patients with cancer ranged from 9.6-92.8%. Lau *et al* (4) performed a meta-analysis of the incidence of DRPs in patients with dementia by collecting data from six public datasets, and the results indicated that the incidence of DRPs in patients with dementia was 19%. In another study targeting home-dwelling patients, it was revealed that the average number of DRPs per individual could reach 4.16 (5). Regarding pediatric patients, Rashed *et al* (6) conducted a statistical analysis of DRPs in children from the Hong Kong region and found that the incidence of DRPs in pediatric patients was 21%, which was higher than that in adult patients overall (6,7). Clinical pharmacists, as patient-centered pharmaceutical care professionals, are responsible for identifying, analyzing and resolving DRPs (8-10). Since the 1990s, pharmacists have employed classification systems to achieve comprehensive and standardized qualitative management of DRPs. At present, no universally accepted classification system exists, but the most widely used schemes are the Pharmaceutical Care Network Europe (PCNE) taxonomy (11) and the Strand classification system (12). Research on DRPs in China is still

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in its infancy. Nevertheless, in 2022, the Shanghai Hospital Association released the first national classification system, the Chinese Drug-Related Problem Classification System (version 1.0) (13). However, previous domestic studies have predominantly focused on adult populations and have largely adopted foreign DRP classification systems (14-18). Investigations specifically addressing pediatric patients remain limited.

The prevalence of chronic kidney disease (CKD) in children globally is estimated to range from 14.9-118.8 per million (19). Epidemiological research on CKD in China is still developing; however, given the large population base and the uneven distribution of medical resources across different regions in China, CKD is characterized by high prevalence, high mortality rates and low levels of awareness among the general population (20). In addition, patients with early-stage CKD often exhibit no notable clinical symptoms, which renders them prone to being overlooked or misdiagnosed during medical visits. This is particularly true for pediatric patients, who are more likely to experience the occurrence of DRPs (21). Ibrahim *et al* (22) reported that, in pediatric nephrology units, the incidence of DRPs among children with CKD is substantial and markedly higher in inpatients than in outpatients (51.2 vs. 32.0%, respectively). The treatment of pediatric CKD is a prolonged, continuous process; complete recovery during hospitalization is rare, necessitating sustained post-discharge therapy (23,24). Following discharge, the absence of a supervised environment often leads to declining adherence over time. Moreover, omissions or administration errors are common since young patients mainly depend on caregivers for medication administration, further predisposing them to DRPs. Additionally, patients referred from external hospitals may have incomplete medication histories, resulting in DRPs, such as therapeutic duplication or drug-drug interactions (25,26). For pediatric patients with CKD, the occurrence of DRPs can have adverse effects on their prognosis and quality of life, such as disease progression, a decreased quality of life, increased hospitalization rates, prolonged periods of hospitalization and increased treatment costs (27-32). Therefore, there is an urgent need to conduct research on DRPs in pediatric patients with CKD, to identify common types and causes of DRPs, and to provide references for the treatment and management of CKD. At present, to the best of our knowledge, no studies have systematically investigated DRPs in Chinese children with CKD.

The present study prospectively collected clinical data on pediatric patients with CKD from the Guiyang Maternal and Child Health Care Hospital (Guiyang, China) to determine the incidence of DRPs in this population and to characterize their types and underlying causes. Furthermore, the impact of clinical-pharmacist interventions on DRPs was evaluated to inform the development of evidence-based pharmaceutical care models for chronic disease management in children.

Patients and methods

Participants and baseline characteristics. The present single-center study was conducted at the Guiyang Maternal and Child Health Care Hospital. Clinical encounters of pediatric patients with CKD between January 1 and December 31 2023

were collected. The inclusion criteria were as follows: i) Aged 0-18 years; ii) patients with CKD at stages 1-5; and iii) the use of ≥ 1 medication (medications used for therapeutic purposes, including vitamin supplements) prior to admission for the purpose of comparing pre- and post-admission differences in medication administration and identifying possible DRPs. A total of 481 patients initially met these criteria. However, the following exclusion criteria were also applied: i) an incomplete medication history; and ii) the inability to communicate effectively with the patient or legal guardian. The final analytical cohort included 383 individuals through the exclusion process. A flow diagram of participant recruitment is provided in Fig. 1. The study protocol was approved by the Guiyang Maternal and Child Health Care Hospital Ethics Committee (approval no. 2022-25) and was conducted in accordance with The Declaration of Helsinki (World Medical Association, 2002).

Within 24 h of admission to the pediatric nephrology ward, a structured data-collection form (admission medication reconciliation/review sheet) was completed for each patient with CKD. The following information was prospectively recorded: demographic data (name, sex, age, date of admission and diagnosis upon admission), previous medical history and complete pre-admission medication history.

PCNE classification. The present study employed the PCNE DRP classification system [version 9.1 (v9.1)] as the primary taxonomy. To enhance its applicability to the study population, the original PCNE v9.1 was modified following a careful review of physician order-check records and documented clinical-pharmacist interventions. Revisions consisted chiefly of the addition of several causative sub-categories for DRPs. In brief, codes C1.7, C1.8, C7.11-C7.17 and C8.2 were newly appended to the PCNE (v9.1).

Identification and classification of DRPs. MR was performed for all in-patients with pediatric CKD. Potential DRPs were identified, their underlying causes were analyzed, and targeted interventions were proposed to both prescribers and caregivers; each identified DRP was subsequently coded using the modified PCNE v9.1 framework.

Statistical analysis. Continuous variables that conformed to a normal distribution were presented as mean \pm standard deviation (SD), whereas those that did not were expressed as median and interquartile range (IQR). Categorical variables were expressed as percentages. Variables with a normal distribution were analyzed using the two-tailed, paired Student's t-test, whereas those failing normality were compared using the Mann-Whitney U test. Categorical variables were analyzed using the χ^2 test by default; for categorical variables that did not meet the assumptions of the χ^2 test, the Fisher's exact test was employed for statistical analysis. Two-tailed $P < 0.05$ was considered to indicate a statistically significant difference. All statistical analyses were performed using R software version 4.5.1 (RStudio, Inc.).

Results

Baseline characteristics of pediatric patients with CKD. A total of 383 children met the predefined inclusion criteria.

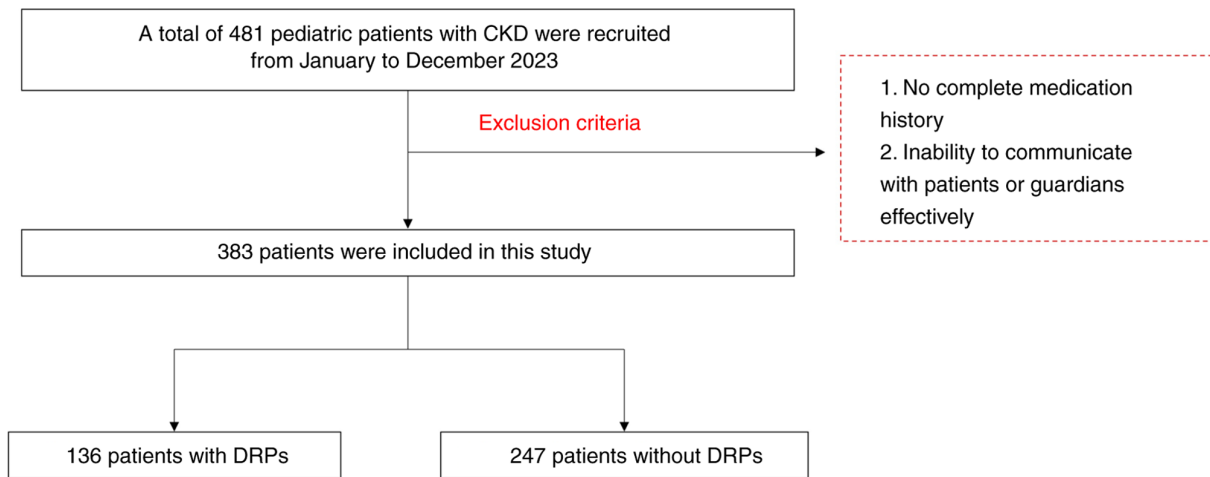


Figure 1. Flowchart of the present study. CKD, chronic kidney disease; DRPs, drug related problems.

The cohort comprised 205 male patients (53.52%) and 178 female patients (46.48%). Distribution by CKD stage was as follows: Stage 1, 303 patients (79.11%); stage 2, 17 (4.44%); stage 3, 21 (5.48%); stage 4, 3 (0.78%); and stage 5, 39 (10.18%) patients. A total of 78 children (20.37%) were receiving ≥ 8 concurrent drugs. The median of hospitalization was 4 days and 62 patients (16.19%) were hospitalized for ≥ 10 days. In addition, 292 (76.24%) patients had been previously admitted for CKD management at least once during the study period.

Occurrence of DRPs. Among the 383 enrolled patients, 136 (35.51%) experienced at >1 DRP (Table I). Within this subgroup, 71 patients were male (52.21%) and 65 were female (47.79%); the median of ages in these patients was 11.1, the median duration of hospitalization was 4.0 days, and the median number of prescribed medications was 6.0. Notably, all 136 patients who developed DRPs had been readmitted at least once. Among these variables, age, comorbidity, the number of medications and hospital readmission were significantly associated with the occurrence of DRPs.

The classification of identified DRPs is presented in Fig. 2. According to the PCNE Classification for DRPs v9.1, DRPs are grouped into three primary domains: P1 (treatment effectiveness), P2 (treatment safety) and P3 (other). P1 indicates a (potential) issue arising from the absence or insufficiency of the pharmacotherapeutic effect; P2 indicates that the patient is experiencing or is at risk of developing an adverse drug event; and P3 indicates miscellaneous issues, such as unnecessary drug therapy or an unclear/unspecified issue or complaint. In the present study, the majority of DRPs fell within domain P1 (treatment effectiveness). Specifically, 108 DRPs were coded as P1.2 (sub-optimal drug effect) and 82 as P1.3 (untreated symptom or indication). In addition, eight DRPs were categorized as P2.1 [(potential) adverse drug event] and five as P3.1 (unnecessary drug treatment).

Causes of DRPs. The related factors underlying the identified DRPs are presented in Table II. Regarding C1.7, ‘Drug is not discontinued promptly despite resolution of

the indication’, continuation of a drug following a cure offers no further benefit and exposes the patient to needless adverse effects and economic cost; a typical example is the prolonged use of hepatoprotective agents following liver-enzyme normalization. Concerning C1.8, ‘Incorrect prescription due to similar medicine names’, names that look or sound alike frequently mislead prescribers; for example, a child on vitamin A + D drops may erroneously receive a prescription for vitamin D drops alone. Categories C7.11-C7.17 capture patient-related factors that are not explicitly itemized in the PCNE framework, such as the following: Self-administration of the wrong product due to name similarity, the unintentional omission of drugs amid polypharmacy, and medication errors or non-adherence resulting from inadequate caregiver supervision. Similarly, C8.2 refers to disruptions caused by a change of healthcare setting (such as transfer from an outpatient clinic to an inpatient ward), leading to erroneous or missed dosing. By incorporating these additional descriptors, the PCNE system can be refined to permit more precise identification and classification of DRPs in the present pediatric CKD cohort.

Drug-selection issues constituted the largest category (n=79), followed by patient-related factors (n=72), dose-selection issues (n=57), drug-use process errors (n=10) and care-transition failures (n=5).

DRP interventions and acceptance. In response to the 223 identified causal factors, 254 discrete interventions were proposed; 243 (95.67%) were fully accepted and executed (Table III). These were stratified by the intervention level as follows: 112 (44.10%) were addressed to prescribers, of which 107 were fully implemented (acceptance rate 95.54%); 49 (19.29%) targeted patients or caregivers, with 45 fully implemented (91.84%); and 93 (36.61%) pertained to the drug product, with 91 fully implemented (97.85%).

Post-intervention outcomes. Among the 136 patients with identified DRPs, the underlying causes were completely resolved in 243 instances (95.67%); 11 cases (4.33%) remained unresolved.

Table I. General information of participants in the present study.

Parameter	No DRPs (n=247)	DRPs (n=136)	P-value
Age, years	9.1 (6.0, 11.9)	11.1 (7.3, 13.0)	0.005
Age, years			0.123
≤6	64 (25.9)	25 (18.4)	
>6	183 (74.1)	111 (81.6)	
Sex,			0.782
Female	113 (45.7)	65 (47.8)	
Male	134 (54.3)	71 (52.2)	
Hospital time, days	4.0 (3.0, 8.0)	4.0 (3.0, 7.0)	0.952
Hospital time, days			0.191
<10	202 (81.8)	119 (87.5)	
≥10	45 (18.2)	17 (12.5)	
CKD			0.712
1	199 (80.6)	104 (76.5)	
2	11 (4.5)	6 (4.4)	
3	13 (5.3)	8 (5.9)	
4	1 (0.4)	2 (1.5)	
5	23 (9.3)	16 (11.8)	
Number of comorbidities	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	0.009
Number of medications	6.0 (4.0, 7.0)	6.0 (5.0, 7.2)	0.035
Number of medications			0.124
<8	203 (82.2)	102 (75.0)	
≥8	44 (17.8)	34 (25.0)	
Hospital readmission			<0.001
No	91 (36.8)	0 (0.0)	
Yes	156 (63.2)	136 (100.0)	

Data are presented as median (IQR) or n (%). DRPs; drug related problems; CKD, chronic kidney disease; IQR, interquartile range.

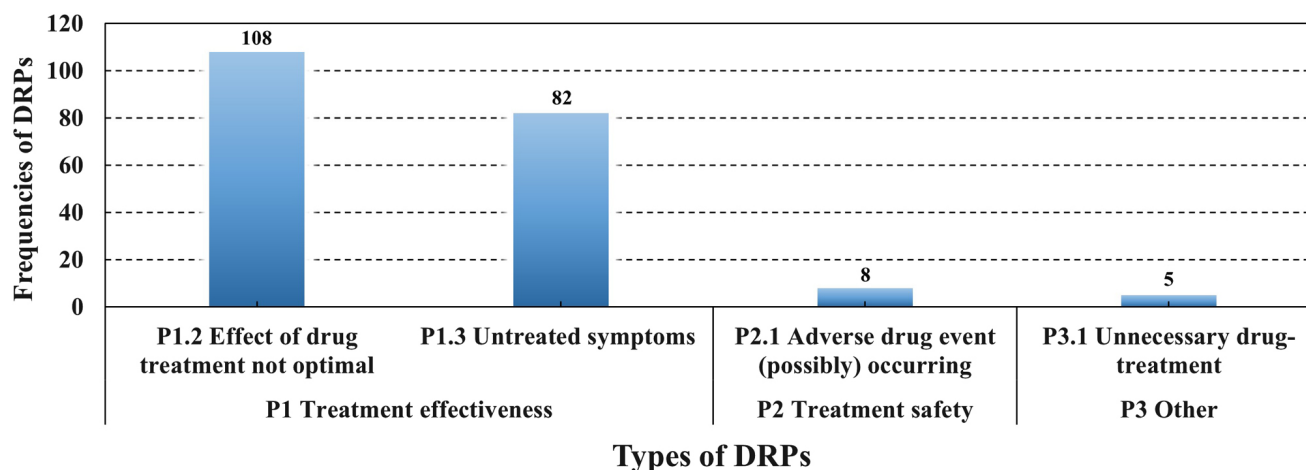


Figure 2. Types of DRPs for pediatric patients with chronic kidney disease at Guiyang Maternal and Child Health Care Hospital (Guiyang, China). DRPs, drug related problems.

Discussion

Pediatric patients often have difficulty adhering accurately to prescribed regimens due to limited swallowing capacity

and under-developed autonomy; consequently, medication administration typically depends on a caregiver. In a previous study, Zhang *et al* (33) applied the PCNE taxonomy to 914 patients with CKD and reported that ‘Treatment safety’

Table II. Causes of drug-related problems based on the revised PCNE classification.

Primary domain	Category	Number of cases	Proportion, %	
C1, Drug selection	C1.4 Inappropriate duplication of therapeutic group or active ingredient	1	0.45%	
	C1.5 No or incomplete drug treatment in spite of existing indication	66	29.60%	
	C1.7 Drug is not discontinued promptly despite resolution of the indication ^a	2	0.90%	
C3, Dose selection	C1.8 Incorrect prescription due to similar medicine name ^a	10	4.48%	
	C3.1 Drug dose too low	17	7.62%	
	C3.2 Drug dose of a single active ingredient too high	9	4.04%	
	C3.3 Dosage regimen not frequent enough	23	10.31%	
C6, Drug use process	C3.4 Dosage regimen too frequent	8	3.59%	
	C6.1 Inappropriate timing of administration or dosing intervals by a health professional	7	3.14%	
	C6.2 Drug under-administered by a health professional	2	0.90%	
	C6.5 Wrong drug administered by a health professional	1	0.45%	
C7, Patient related	C7.1 Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	21	9.42%	
	C7.2 Patient uses/takes more drug than prescribed	9	4.04%	
	C7.4 Patient decides to use unnecessary drug	6	2.69%	
	C7.7 Inappropriate timing or dosing intervals	11	4.93%	
	C7.11 Incorrect medication due to the patient self-purchasing ^a	6	2.69%	
	C7.12 Medication not administered due to depletion of the supply ^a	7	3.14%	
	C7.13 Incorrect medication due to similar medicine name ^a	4	1.79%	
	C7.14 Non-adherence to prescription due to excessive medication use ^a	1	0.45%	
	C7.15 Medications not taken regularly due to the lack of the medication supervisor ^a	5	2.24%	
	C7.16 Medication supervisor forgets to supply medication ^a	1	0.45%	
	C7.17 Incorrect medication due to the change of medication supervisor ^a	1	0.45%	
	C8, Patient transfer related	C8.2 Patient takes an incorrect medication or does not take medication due to a change in care institution ^a	5	2.24%

^aCategories were added to the PCNE (version 9.1) according to causes identified in pediatric patients with chronic kidney disease at the Guiyang Maternal and Child Health Care Hospital (Guiyang, China). PCNE, Pharmaceutical Care Network Europe.

Table III. Interventions made by pharmacists, acceptance and outcomes of intervention proposals classified by the Pharmaceutical Care Network Europe version 9.1.

Primary domain	Types of intervention/implementation/outcomes	Number of cases, n	Proportion, %
I1, At prescriber level	I1.1 Prescriber informed only	36	14.17%
	I1.3 Intervention proposed to prescriber	69	27.17%
	I1.4 Intervention discussed with prescriber	7	2.76%
I2, At patient level	I2.2 Written information provided (only)	3	1.18%
	I2.4 Spoken to family member/caregiver	46	18.11%
I3, At drug level	I3.1 Drug changed to ...	9	3.54%
	I3.2 Dosage changed to ...	29	11.42%
	I3.4 Instructions for use changed to ...	29	11.42%
	I3.5 Drug paused or stopped	9	3.54%
	I3.6 Drug started	17	6.69%
A1, Intervention accepted	A1.1 Intervention accepted and fully implemented	243	95.67%
	A1.2 Intervention accepted, partially implemented	3	1.18%
	A1.3 Intervention accepted but not implemented	6	2.36%
A2, Intervention not accepted	A2.2 Intervention not accepted: no agreement	2	0.79%
O1, Solved	O1.1 Problem totally solved	243	95.67%
O3, Not solved	O3.1 Problem not solved, lack of cooperation of patient	3	1.18%
	O3.2 Problem not solved, lack of cooperation of prescriber	8	3.15%

was the predominant DRP domain, followed by ‘Treatment effectiveness’. This hierarchy diverges from the findings of the present study and is probably attributable to the distinct demographic profile of their study cohort. In the present study, MR identified DRPs that were predominantly attributable to drug selection, patient-related factors and dose selection; specifically, 66 DRPs arose from untreated or incompletely treated indications, 23 from sub-optimal dosing frequency and 21 from under-dosing or non-administration of prescribed doses. In a previous study, Zafar *et al* (34), employing the PCNE framework in patients from Pakistan with CKD, identified ‘inappropriate drug selection’ as the most common root cause of DRPs; an identical pattern was also reported in a separate cohort that consisted of 269 pre-dialysis patients recruited from the nephrology ward of Ibni Sina Hospital, Ankara University School of Medicine (Ankara, Turkey) between October 2019 and March 2020 (35). These findings suggest that lapses in caregiver or self-supervision serve a key role; compared with adults, children exhibit a poorer comprehension of medication use and, in the event that the caregiver lacks adequate medication literacy or no consistent caregiver is available, safety and effectiveness cannot be assured (36,37).

Patients with chronic diseases are frequently re-hospitalized and among the 383 children enrolled in the present study, 292 were repeat patients, of which 136 experienced DRPs; conversely, no DRPs were observed in first-time patients. Additionally, the ‘hospital readmission’ variable displayed a significant association with the occurrence of DRPs, indicating that repeated admissions may introduce gaps in medication histories, particularly in pediatric patients, leading to incomplete information at admission and subsequent DRPs. Moreover, patients who experienced DRPs were significantly older, had more comorbidities and were exposed to more concomitant medications. By contrast, the duration of hospitalization and CKD stage did not exert significant effects on the risks of developing DRPs. Unexpectedly, a non-significant trend toward a higher DRP rate was observed among children with a shorter duration of hospitalization. Pehlivanli *et al* (35) reported that DRPs were associated with a prolonged duration of hospitalization, which may reflect age-specific care dynamics: Extended periods of hospitalization in pediatric units may facilitate intensive pharmaceutical stewardship, thereby attenuating the occurrence of DRPs. Nevertheless, the absence of a statistically significant duration of hospitalization between groups in the present study may stem from

limited statistical power; the multi-center enlargement of the cohort is warranted to clarify the true association between the duration of hospitalization and DRPs in children with CKD. Notably, patients with CKD in the early stages (particularly stage 1) face disproportionate medication-management challenges. The present study hypothesized that these patients often perceive their illness as trivial, resulting in an inadequate appreciation of treatment complexity and the critical importance of adherence. Frequent therapeutic adjustments, repeated admissions and inter-facility transfer further magnify the probability of prescribing errors, duplication or omissions. Thus, clinical pharmacists could compare physician orders with patient-reported use, perform MR, identify potential issues, rationalize dosing schedules, revise medication lists, and thereby mitigate medication-related risks and enhance the safety of patients with CKD.

In 2022, the Shanghai Hospital Association and the Shanghai Pharmaceutical Association released the Chinese Drug-Related Problem Classification System (version 1.0). Compared with the PCNE taxonomy, this system adds a 'DRP evaluation' domain requiring explicit coding of 'E1 primary subject' and 'E2 DRP severity' and introduces 'C7 information systems and devices' under causes, while adjusting several other items; however, its target population is adults. As the cohort in the present study comprised children, certain categories in the Chinese system were not applicable. During the pilot phase of the present project, the original PCNE classification system was first applied to 100 pediatric in-patients and it was revealed that several root causes of DRPs could not be adequately coded. On the basis of these preliminary data, a revised version of the PCNE system was developed that could provide exhaustive categories for the present study population. Accordingly, in the present study, the PCNE (v9.1) was adapted to reflect local pediatric practice, focusing on the causal domain and adding 10 new codes. Multicenter validation of the modified PCNE system is nevertheless required in future work to confirm its reliability and generalizability for detecting DRP causes in Chinese children.

During the present MR study, several deficiencies and misconceptions among medication caregivers were identified. Typical examples included the following: i) the omission or incorrect administration of drugs due to polypharmacy and the absence of a dedicated caregiver (such as a patient prescribed nine concurrent medications failed to take hydroxychloroquine and mycophenolate mofetil); ii) the substitution of prescribed therapy with nutraceuticals of uncertain composition (for example, caregivers purchased unlabeled calcium supplements instead of the prescribed calcium preparation, resulting in persistent hypocalcemia); iii) dose discrepancies arising from transitions of care (such as an outpatient instruction to taper prednisone according to weekly urinalysis was misinterpreted; thus, the dose on readmission differed from the intended regimen); iv) the intentional omission of chronic therapy at admission (for example, enalapril was withheld without justification); v) the administration of doses exceeding the manufacturer's labeled maximum; and vi) the continuation of therapy after the indication had resolved. Consequently, clinical pharmacists could use the study-specific, pediatric-adapted PCNE (v9.1) to rapidly classify DRPs and their causes, and to design targeted interventions, such as regimen

simplification, caregiver education, written action plans and psychological support, which could enhance both the efficacy and the safety of pharmacotherapy.

The present MR initiative successfully identified and addressed DRPs in children with CKD, providing a replicable model for pediatric chronic disease management. Nevertheless, several limitations should be acknowledged. First, the modifications to the PCNE v9.1 were derived solely from a single-center cohort, and external validity across institutions and pediatric chronic conditions remains to be established through multicenter studies. Second, long-term outcomes, particularly sustained adherence and disease control, were not evaluated. Future research is thus warranted to expand the research to diverse geographic regions and hospital tiers to enhance generalizability and incorporate prospective follow-up to assess the impact of pharmaceutical care on long-term prognosis, including disease progression and quality of life.

In conclusion, the implementation of comprehensive pharmaceutical care throughout the continuum of chronic disease management represents an inevitable trajectory for the advancement of pharmacy practice. The present study explored a MR model tailored to pediatric patients with CKD and further refined the PCNE v9.1 taxonomy to enable more accurate classification of DRPs in this population. These enhancements facilitate the development of individualized interventions.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XJ contributed to the project administration, conceptualization, and reviewed and edited the manuscript. WY contributed to the study conceptualization, project administration, methodology, and reviewed and edited the manuscript. XL wrote the original draft, made substantial contributions to conception and design, and was a project administrator. YL contributed to the curation, formal analysis and investigation of data. ZM designed the methodology and supervised the study. XW curated the data, designed the methodology and created figures. SZ contributed to the investigation, data curation and methodology. QH contributed to the methodology, formal analysis of data and creating figures. JL contributed to the data curation, methodology and investigation. YZ reviewed and edited the manuscript and contributed to the curation of data. SL contributed to the resources, curation of

data and investigation. BC reviewed and edited the manuscript, made substantial contributions to conception and design, and contributed to the methodology. YH contributed to statistical analysis, supervision, and creating figures. XJ and XL confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study protocol was approved by the Guiyang Maternal and Child Health Care Hospital Ethics Committee (approval no. 2022-25) and was conducted in accordance with The Declaration of Helsinki (World Medical Association, 2002). The parents or guardians of all participants provided their written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, an AI tool (Kimi) was used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the AI tool as necessary, taking full responsibility for the ultimate content of the present manuscript.

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