"Impact of Polypharmacy on Disease Status and Medication RelatedQualityofLifeAmongPatientswithChronicKidney Disease"

DarshanBelagali[1],GeetanjaliSalimath[2*],GangayyaWakkundmath[3],SamarthAnigol[4], Mallikarjun Karishetti [5]

[1,2*,3,4,5]Dept. of PharmacyPractice, KLE college of pharmacy, Airport Road, Basavan Kudachi, Belagavi-591124 KLE Academy of Higher Education and research, (KAHER) Belagavi-590010 Karnataka, India
[5]Dept.of Nephrology, JNMedicalcollege, NehruNagar, Belagavi-590010, Karnataka,India.

Correspondence: Dr.GeetanjaliSalimath
Department of Pharmacy Practice, KLE college of pharmacy, Airport Road, Basavan Kudachi, KLE Academy for higher education and research centre, Belagavi-591124, Karnataka, India.
E-mailid:geetanjalisalimath@klepharm.edu

ABSTRACT:

Background

Chronic kidney disease (CKD) is a progressive noncommunicable disease affecting approximately 788 million persons worldwide. Polypharmacy, defined as the concurrent use of five or more medications, is highly prevalent among CKD patients due to coexisting comorbidities including hypertension, diabetes mellitus, cardiovascular disease, anaemia, and mineral bone disorders. Despite its clinical significance, limited prospective evidence exists assessing the combined impact of polypharmacy on disease status, adverse events, and quality of life, particularly within the Indian healthcare context.

Objective

To assess the effect of polypharmacy on disease status and medication burden-related quality of life (MRQOL) inpatients with CKD.

Methods

A cross-sectional study was conducted in the Nephrology ward and General Medicine departments at Tertiary care teachinghospital,Belagavi, overeightmonths.Atotal of 136CKDpatients(Stages1–5,includingdialysis)aged18 years or older and taking five or more concurrent medications were enrolled. Data on sociodemographic characteristics,clinicalparameters,medicationprofiles,adverseevents,andMRQOLwerecollected.TheMedication-Related Quality of Life (MRQOL) questionnaire was administered. Data were analysed using SPSS software; multinomial logistic regression was used to identify independent predictors of medication burden.

Results

The majorityof patients (46.3%) were aged 41–60 years, 58.1% were male, and 60.3% had Stage 5 CKD. Moderate polypharmacy (5–9 drugs) was detected in 45.6% of patients, while severe polypharmacy (>9 medications) was identified in 21.3%, yielding an overall clinically relevant polypharmacy rate of 66.9%. Educational status was significantlyassociated with polypharmacy($p<0.001$), with 51.7% of illiterate patients having severe polypharmacy compared to 6.9% of graduates. Regarding MRQOL, 42.6% of patients experienced minimal burden, while 32.3% reported clinically significant impairment. The social and lifestyle domain was most adversely affected. A highly significant association was found between polypharmacy and medication burden-related quality of life ($p=0.0001$). Multinomiallogisticregressionconfirmedpolypharmacyasanindependentpredictor ofimpairedQoL,withpatients on 2–4 drugs having significantly lower odds of noticeable medication burden (OR=0.006; 95% CI: 0.001–0.057; $p<0.001$) compared to those on more than nine medications.

Conclusion

PolypharmacyiscommonamongCKDpatientsandsignificantlyimpairsmedication-relatedqualityoflifeinadose-dependent manner. Educational status is a key predictor of polypharmacy severity. Routine medication review, deprescribing strategies, patient education, and pharmacist-led interventions are essential to optimise pharmacotherapy and improve patient outcomes in CKD.

Keywords: Polypharmacy; Chronic Kidney Disease; Medication-Related Quality of Life; MRQOL; Adverse Drug Events; Deprescribing; Pharmacist Intervention
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INTRODUCTION

Chronickidneydisease(CKD)hasemergedasone of themostseriousnoncommunicablediseasesofthe contemporaryperiod,imposingamassiveandgrowing burden on global health systems. According to the Global Burden of Disease (GBD) Study 2023, approximately788millionpersonsworldwidewere estimated to have CKD in 2023, more than doubling the378millioncasesrecordedin1990.Theglobal age-standardizedprevalencecurrentlystandsat 14.2%,reflectinga3.5%increaseoverthreedecades.[1]I n2023,CKDwastheninthleadingcause ofdeathworldwide,accountingfor1.48milliondeaths annually, and the twelfth leading cause of disability-adjustedlifeyears(DALYs).[1]Type2diabetes mellitus,systemichypertension,obesity,andan ageingglobalpopulationaretheprimarydriversofits increasedoccurrence,withtheconditionultimately progressingtoend-stagerenaldisease(ESRD) requiring renal replacement therapy.[1,2]

Polypharmacyisawidelyusedclinicaltermwithouta universallyacceptteddefinition,resultinginvariability inhowitisreportedandquantifiedacrossstudies.The most commonly applied threshold defines polypharmacy as the concurrent use of five or more medications by a single patient.[3] Hyper polypharmacy,definedastheuseoftenormore medicationssimultaneously,isassociatedwitha significantlyelevatedriskof drug-relatedharm.[3,17]

Itiscriticaltodistinguishbetween'appropriate polypharmacy',whereconcurrentuseofmultiple medicationsisclinicallyjustifiedandevidence-based, and'problematicpolypharmacy',whereoneor more medicationsareunnecessary,duplicative,dose-inappropriatelyprescribed,orpotentiallyharmful giventhepatient'srenalfunctionandclinicalcontext.[19]

CKD is characterised by a series of systemic complications that worsen with disease progression. As estimated glomerular filtration rate (eGFR) declines, patients develop anaemia of chronic kidney disease, metabolic acidosis, hyperkalemia, fluid overload, secondary hyperparathyroidism, CKD-mineral and bone disorder (CKD-MBD), and heightened cardiovascular disease (CVD) risk.[22]

Cardiovasculardiseaseistheleadingcauseofdeathin CKD patients, driven by both traditional risk factors and CKD-specific mechanisms including uraemic toxin accumulation, endothelial dysfunction, and systemicinflammation.[2,22]The combined burdenof these multi-system comorbidities necessitates simultaneousprescriptionofnumerousdrugs,directly contributing to the clinical problem of polypharmacy.[8]

Polypharmacy is an increasingly widespread global problem.Alargecross-sectionalanalysisofWave9of the Survey of Health, Ageing, and Retirement in Europe(SHARE),encompassingparticipantsfrom27 European countries and Israel, reported an overall polypharmacy prevalence of 36.2% among older adults aged ≥65 years, ranging from 25.0% to 51.8% across participating countries.[3] Advanced age, female sex, a higher number of chronic conditions, multimorbidity, and lower socioeconomic position were identified as significant independent predictors.[3]

In CKD patients, polypharmacy is linked to adverse drug reactions, drug-drug interactions, medication non-adherence, medication errors, increased hospitalisation, and elevated healthcare expenditure. Impairedrenalfunction altersthe pharmacokinetic and pharmacodynamic profiles of many medications, rendering CKD patients more vulnerable to side effects and drug toxicity. As CKD severity worsens, the number of prescription drugs typically increases, furtherraisingthe riskof medication-related problems. [8,9]

Polypharmacyalsohasasubstantialimpactonhealth-relatedqualityoflife(HRQoL)inCKDpatients.High pill burden, complex dosing schedules, dietary restrictions,drugsideeffects,andlong-termtreatment demands can negatively influence physical, psychological, social, and emotional well-being, thereby limiting treatment adherence and influencing disease outcomes.[14,15] Despite the clinical significance of these interrelated outcomes, few studies have simultaneously assessed disease status, safety outcomes, and quality of life in CKD-specific populations, particularly within the Indian healthcare context. Thisstudyaimstoaddressthatevidence gap.

METHODOLOGY

ThestudywasconductedintheNephrologywardand General Medicine departments at Tertiary care teaching hospital, Belagavi, Karnataka, India. This investigation was conducted using a cross-sectional observationalstudydesign.Datacollection:8months Data analysis and manuscript preparation: 1-month Patientsdiagnosedwithchronickidneydisease(CKD) attendingtheNephrologywardandGeneralMedicine departmentswerethetargetpopulation.Inclusion

criteria is Patients diagnosed with chronic kidney diseaseStages1–5orthosereceivingdialysis.Patients taking five or more medications concurrently. Adults aged 18 years or older. Exclusion criteria is Patients who provided written informed consent to participate in the study. Patients with cognitive impairment that prevents completion of surveys or provision of informed consent.

StudyProcedure

Ethicalapprovalwasobtainedpriortocommencement of the study. Patients attending the Nephrology ward and General Medicine departments were screened basedontheinclusionandexclusioncriteria.APatient Information Sheet was provided to all eligible participants in their preferred language. Written informed consent was obtained from all participants before enrolment.

Sociodemographic data (age, sex, educational status, occupation), clinical data (CKD stage, comorbidities, laboratory parameters), and complete medication profiles were collected using a structured data collection form. The MRQOL questionnaire was administered to assess the impact of medication burden onqualityof lifeacrossmultiple domains.All data were entered into a structured database for analysis.

DataAnalysis

Data were analyzed using SPSS (Statistical Package for theSocial Sciences)software.Descriptive statistics were used to summarize sociodemographic and clinical variables. Chi-square tests were performedto assess associations between categorical variables. Multinomial logistic regression analysis was used to identifyindependentpredictorsofmedicationburden-related quality of life. A p-value of <0.05 was considered statistically significant.

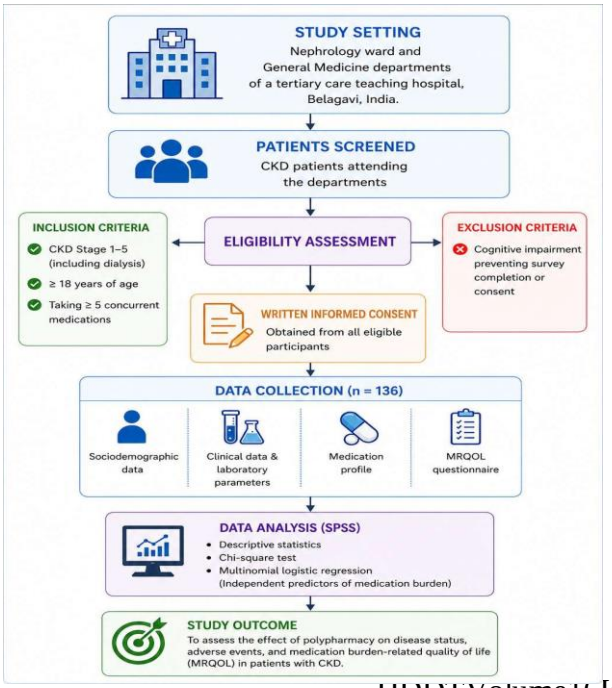
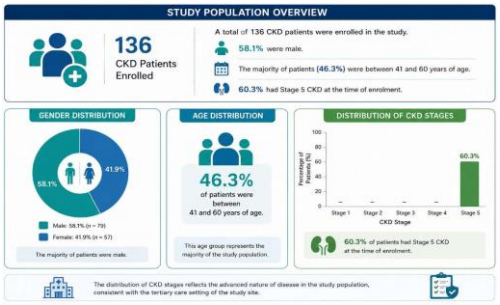


Figure 1. Study methodology flowchart showing patient recruitment, eligibility assessment, data collection, and statistical analysis.

RESULTS

SociodemographicProfile

Atotalof136CKDpatientswereenrolledinthestudy.



Themajorityofpatients(46.3%)werebetween41and 60 years of age, 58.1% were male, and 60.3% had Stage5CKDatthetimeofenrolment.Thedistribution of CKD stages reflected the advanced nature of disease in the study population, consistent with the tertiary care setting of the study site.

Figure 2. Study population characteristics.

Prevalence and Pattern of Polypharmacy Moderatepolypharmacy(5–9concurrentmedications) wasobservedin45.6%ofpatients,whilesevere polypharmacy(morethan9medications)wasidentifiedi n21.3%ofpatients,yieldinganoverall clinicallyrelevant polypharmacyprevalence of 66.9%. Theremaining33.1%ofpatientswereclassifiedas havingminorpolypharmacy(2–4drugs).These findingshighlightthesubstantialmedicationburden borne by CKD patients in the study cohort.

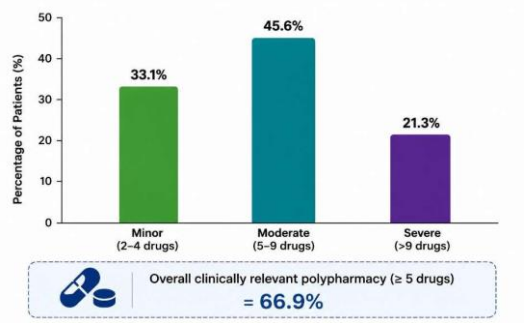


Figure 3. Distribution of polypharmacy severity among CKD patients.

Association Between Sociodemographic Factors and Polypharmacy

The relationship between CKD stage and polypharmacy was not statistically significant (p=0.154);however,severepolypharmacywasmost

prevalent among Stage 5 patients (69.0%), indicating a clinically meaningful trend towards increasing medication burden with advancing disease.

Educational status was significantly associated with polypharmacy (p<0.001). Among illiterate patients, 51.7% had severe polypharmacy, compared to only 6.9% of patients with graduate-level education. Occupation was also significantly associated with polypharmacy (p=0.023), suggesting that socioeconomicfactorsinfluencetreatmentcomplexity and healthcare utilization.

Variable	Category	p-value
CKDStagevs. Polypharmacy	Stage5–severe polypharmacy 69.0%	0.154
Educational Status vs. Polypharmacy	Illiterate – severe 51.7%; Graduate – severe 6.9%	<0.001
Occupationvs. Polypharmacy	Significant association	0.023

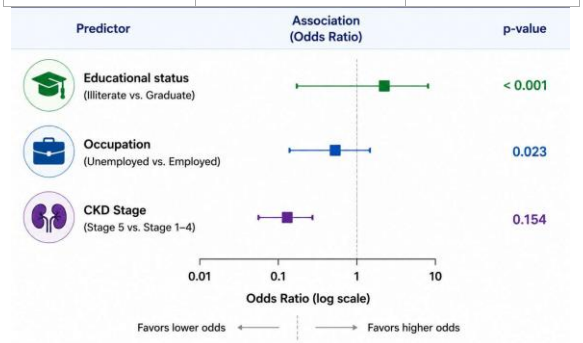


Figure 5. Significant predictors associated with polypharmacy.

Medication Burden-Related Quality of Life (MRQOL)

Assessment of medication burden-related quality of life using the MRQOL questionnaire revealed that 42.6%ofpatientsexperiencedminimalburden,25.1% reported a slight burden, and 32.3% experienced clinicallysignificantimpairment(noticeableorsevere burden).Thesocialandlifestyledomainwasthemost adversely affected, with only 23.5% of patients reporting minimal hardship in this area and 7.4% reportingaconsiderableburden.Medicationusehada notable impact on social activities, travel, and family engagement.

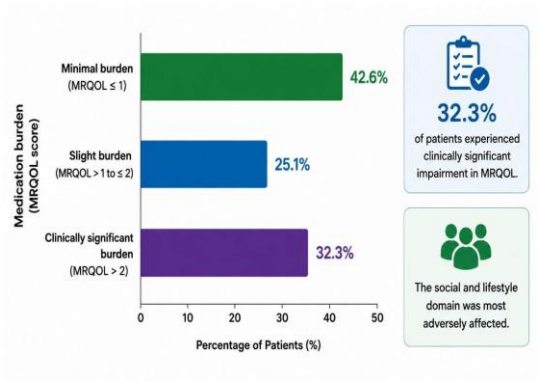


Figure4.Distributionofmedicationburden-related quality of life (MRQOL).

Association Between Polypharmacy and MRQOL

Astatisticallyhighlysignificantassociationwas observedbetweenthenumberofmedicationsand medication burden-related quality of life (p=0.0001). Patientsusing 2–4 drugs reported the lowest burden (55.2% minimal burden), whereas all patients with a high medication burden were those taking more than ninemedications.Thisfindingdemonstratesaclear dose-responserelationshipbetweenincreasingdrug count and declining quality of life.

Medication Count	Minimal Burden (%)	Clinically Significant (%)	p-value
2–4drugs	55.2%	Low	—
5–9drugs	Moderate	Moderate	—
>9drugs	Lowest	Highest	0.0001

MultinomialLogisticRegression

Multinomial logistic regression analysis confirmed polypharmacy as an independent predictor of medicationburden-relatedqualityoflife.Comparedto patients taking more than nine medications, those receiving 2–4 medications had significantly lower odds of experiencing noticeable medication burden (OR=0.006;95%CI:0.001–0.057;p<0.001).Patients on 5–9 medications also had significantly reduced oddsofnoticeableburden(OR=0.040;95%CI:0.005–0.330; p=0.003).

Medication Group	OR	95%CI	p-value
2–4 drugs (vs.>9)	0.006	0.001–0.057	<0.001
5–9 drugs (vs.>9)	0.040	0.005–0.330	0.003

DISCUSSION

The current study examined the effect of polypharmacyonmedicationburden-relatedqualityof life in 136 patients with chronic kidney disease. The majority of patients (46.3%) were aged 41–60 years, 58.1%weremale,and60.3%hadStage5CKD, reflectingthesubstantialglobalburdenofadvanced renal disease, particularlyin low- and middle-income countries.[1,14]Moderatepolypharmacy(5–9drugs) wasdetectedin45.6%ofpatients,whileseverepolypharm acy(>9medications)wasidentifiedin 21.3%,foratotalclinicallyrelevantpolypharmacy prevalence of 66.9%. This rate is significantly higher thanthatreportedinthegeneralolderadultpopulation, underscoringthecomplexityofCKDmanagement, whichfrequentlynecessitatesmultipleagentsto addresshypertension,diabetes,anaemia,mineralbone disorders, and cardiovascular complications. [2,8,9] The relationship between CKD stage and polypharmacy was not statistically significant (p=0.154);nevertheless,severepolypharmacywas most prevalent among Stage 5 patients (69.0%). This findinghasimportantclinicalimplications,asadvancedC KDisassociatedwithincreasedtreatment complexityandaheightenedriskofmedicationaccumula tion,drug-druginteractions,andadverse drugreactions.[10,15]Theseobservationsare consistentwithpriorresearchdemonstratingthat advanced CKD paired with polypharmacy significantly increases mortalityrisk and the prevalence of drug-related problems.[7,8]Educationalstatuswassignificantlyasso ciatedwith polypharmacy(p<0.001).Overhalfofilliterate patients(51.7%)hadseverepolypharmacy,compared toonly6.9%ofgraduates.Thisfindingechoes previousstudiesdemonstratingthatlowereducational attainmentislinkedtopoormedicationadherenceand difficultieswithmedicationself-management,andthat low educational status is an independent predictor of polypharmacyseverity.[2,5]Occupationwasalso significantlyassociatedwithpolypharmacy(p=0.023), indicatingthatsocioeconomicstatusmayinfluence treatment complexity and healthcare utilization.[3] Assessmentofmedicationburden-relatedqualityof liferevealedthat42.6%ofpatientsexperiencedminimalb urden,while32.3%reportedclinicallysignificantimpair ment.Thesocialandlifestyle domainwasthemostadverselyaffected,withonly 23.5% reporting minimal hardship and 7.4% experiencingconsiderableburden.Medicationuse exertedasignificantimpactonsocialactivities,travel, andfamilyparticipation.Thesefindingsareconsistent withpriorstudiesreportingsignificantdeclinesin health-relatedqualityoflifeamongCKDpatients exposedtopolypharmacy,particularlyinsocial functioning domains. [13,18]

Although the correlation between CKD stage and quality of life did not reach statistical significance (p=0.073), Stage 5 patients carried the highest drug burden.Thisalignswithevidencethatseriousadverse drug reactions rise significantly with deteriorating kidney function, and that renal impairment increases the probability of clinically significant drug-drug interactions, contributing to increased treatment burden and poorer patient outcomes.[15]

Themostnoteworthyfindingofthepresentstudywas the highly significant association between polypharmacy and medication burden-related quality oflife(p=0.0001),withacleardose-responsepattern: patientsusing 2–4 drugs reported the lowestburden (55.2%), whereas all patients with a high medication burdenwerethosetakingmorethanninemedications. Similar dose-response relationships between increasing medication count and declining quality of life have been reported in the literature. [3,13] Multinomial logistic regression confirmed polypharmacyasanindependentpredictorofimpaired qualityoflife.Thesefindingsaresupportedbyevidencefr ompharmacist-ledinterventionstudies, includingZafaretal. [11] andthe K-CHAMPtrial by Lavilleetal.[12],whichdocumentedsignificant reductions in medication-related problems and improvements in quality of life following systematic medication review and deprescribing.

CONCLUSION

The present study demonstrates that polypharmacy is highlyprevalentamongCKDpatientsinatertiarycare settingandexertsaconsiderablenegativeinfluenceon medication-relatedqualityof lifeina dose-dependent manner. Educational status emerged as a significant predictor of polypharmacy severity, while increasing medicationcountwasindependentlyandsignificantly associated with declining quality of life across multipledomains,mostnotablythesocialandlifestyle domain.

Thesefindingsunderscoretheurgentneedfor routine medication review, structured deprescribing protocols, patient education tailored to educational level, and pharmacist-led interventions as integral components of CKD management. Such approaches should be implemented in accordance with KDIGO 2024 recommendations to optimise pharmacotherapy, reduce medication-related adverse events, and improve the overall quality of life of CKD patients.

Future studies employing longitudinal designs and incorporating objective clinical outcomes alongside patient-reported outcomes are warranted to further characterise the dynamic relationship between polypharmacy,diseaseprogression,andqualityoflife in CKD.

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