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Prevalence of inappropriate drug dose adjustment and associated factors among inpatients with renal impairment in Africa: A systematic review and meta-analysis

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Abstract

Objective: There is a high prevalence of inadequate dose adjustment among inpatients with renal insufficiency worldwide. There is, however, a paucity of studies that summarizes the topic in the African context. Therefore, this study aims to summarize the prevalence of inappropriate drug dose adjustment (IDDA) and associated factors among inpatients with renal impairment in Africa.

Methods: A literature search for English-language articles was conducted using reputable databases such as PubMed/MEDLINE, Google Scholar, and Science Direct. The search was carried out between 3 February and 3 March of 2022. All published articles that were online at the time of data collection were considered. Observational studies that examined the prevalence of IDDA for any type of drug in renal impairment as a primary or secondary outcome were included in our analysis. Statistical software such as Open Meta Analyst and Review Manager were used to examine outcome measures. I^2 statistics, Logit event rate, and Der Simonian and Laird's random effect models were also used.

Results: Seven articles were qualified for the systematic review and meta-analysis. All included studies comprised a total of 1918 patients. A total of 5072 prescriptions were assessed, and 1879 (37%) of them had at least one drug that required a dose adjustment. The pooled prevalence of IDDA among adult patients with renal impairment was 13.7% (95% confidence interval (CI) = 7.9%–19.5%) in Africa. Based on the number of prescriptions containing medications that required dose adjustment, the pooled prevalence accounts for 39.3% (95% CI = 24.1%–54.4%) (932/1879). Factors associated with inappropriate drug prescribing and usage concerning renal function were the number/types of prescribed medicines (most common), age, stage of renal impairment, comorbidity, and unemployment.

Conclusions: In this study, IDDA practice appears to be a common challenge among inpatients with renal insufficiency in Africa. The number and type of medications prescribed, age, stage of renal impairment, comorbidity, and unemployment were factors associated with inappropriate drug prescribing and use. In addition to expanding such studies, hospitals across Africa must conduct research on the clinical outcomes of IDDA practices in patients with renal impairment.

Keywords

Africa, drug dose adjustment, inappropriate prescribing, renal impairment

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Introduction

The clearance of most drugs including their active metabolites depends on the renal filtration rate, excretion, and reuptake.[1] In renal insufficiency, the elimination of renal excreted drugs is altered and dose adjustment is required for renally impaired patients.[2] Consequently, several drugs and their active metabolites could bring nephrotoxicity or deteriorate renal dysfunction.[3] For example, drugs were responsible for nearly 20% of acute renal injuries that occurred among inpatients and outpatients.[4,5] The incidence of medicine-related kidney injury was higher among older adults (66%).[6]

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Consequently, drug-induced renal toxicity may result in a rise in morbidity and the financial burden of healthcare costs.[7]

However, global reports indicate the high prevalence of inadequate dose adjustment among inpatients with renal insufficiency.[8–10] Several studies have revealed that about 25%–77% of inpatients with renal impairment have used drugs with inappropriately unadjusted doses.[8–12] Several studies have also shown that unadjusted doses are commonly prescribed to renal insufficient patients in developed countries. For example, the prevalence of inappropriate drug dose prescriptions was 11.9% and 35% in USA and France, respectively.[13,14] Likewise, this figure is even higher in lower to middle-income countries. For example, a higher rate of prescribing unadjusted doses was reported in countries such as Pakistan (58.2%), Lebanon (49%), India (63%), and Saudi Arabia (53%).[15–18]

Systematic reviews and meta-analyses combine evidence from various research findings to generate potentially more substantial evidence than individual studies alone.[19] As a result, healthcare practitioners, policymakers, and other key stakeholders could benefit from such type of study in their respective decision-making processes to avoid poor clinical outcomes and toxicity caused by inappropriate drug dose adjustment (IDDA) practices. Consequently, the two most recent systematic reviews Tesfaye et al.[20] and Dörks et al.[21] have studied the topic in the global context. However, no current comprehensive review of the literature has been conducted in the African context to summarize the prevalence of IDDA and associated factors in patients with renal impairment. Therefore, this systematic review and meta-analysis aims to summarize the prevalence of IDDA in patients with renal impairment and to identify factors contributing to inappropriate dose adjustment in African hospitals.

Methods

Study protocol

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) standard was used to report the record identifications, title and abstract screening, and eligibility of full articles for final admission. The PRISMA checklist was also rigorously tracked while reporting this systematic review and meta-analysis (Supplemental PRISMA Checklist).[22] The study protocol can be found on PROSPERO under the reference identification number CDR 42020149416, and the methodology can also be accessed at https://www.crd.york.ac.uk/prospero/display_recored.php?ID=CDR42020149416.

Study eligibility and screening

DD designed the study. Three authors GA, TE, and ZB screened the title and abstracts of the articles following the inclusion and exclusion criteria. GA and TE additionally gathered the full texts, examined the studies' eligibility for final inclusion, appraised the study's quality, then analyzed the data. DD and ZB commented on the review and meta-analysis.

Inclusion and exclusion criteria

Inclusion criteria. This study only considered studies that met the following inclusion criteria. Our study included observational studies in Africa (prospective, retrospective, and descriptive cross-sectional studies) that looked at the prevalence of IDDA in renal impairment as a primary or secondary outcome. Studies that reported on IDDA or utilization of contraindicated medications and evaluated objectively (i.e., based on guidelines, product information, or extent of renal elimination) were also included. Additionally, studies that clearly defined the renal impairment either via equation-based estimates of creatinine clearance (CrCl)/glomerular filtration rate (GFR), or a change in serum creatinine (sCr), with or without additional markers such as proteinuria were included. Studies should include all patients of age 18 or older, patients with renal impairment, and those admitted to a hospital ward taking at least one medication. There was no limit on the publication year of the articles. Studies that were published in the English language and provided other sufficient data for the review were included.

Exclusion criteria. Articles with missing or insufficient outcomes, case reports, comments, letters to the editor, theses, case studies, congress abstracts, reviews, and meta-analyses were excluded from this study. Moreover, articles that merely assess the prevalence or incidence of inappropriate prescribing without describing interventions in dosing adjustment were also excluded. Studies conducted outside of Africa, and those limited to non-hospitalized patients, children, and patients with specific diagnoses or diseases (e.g., dialysis patients or HIV patients), were not part of this review and meta-analysis.

Data sources and search strategy

We looked for English-language articles in reputable databases such as PubMed/MEDLINE, Google Scholar, and Science Direct. We only used English because there is a higher risk of bias in a meta-analysis and it may reduce study heterogeneity.[19] Advanced search strategies were used in Science Direct and HINARI to find any further studies or reviews, as well as to obtain significant findings on the prevalence of IDDA in renal impairment and associated factors among hospitalized patients in African healthcare settings.

The search was carried out using well-chosen search terms with no regard for time restrictions. Such words were dosage/dose adjustment, renal impairment, kidney diseases, renal function, dosing errors, inappropriate prescribing, inappropriate medication, and Africa. The MeSH terms were

also used as follows (each key term followed the same): ("Dose adjustment" [MeSH Terms] OR "Dose adjustment" [Text Word] OR "Dosage adjustment" [Text Word] OR "Dosage adjustment" [Text Word] OR "Inappropriate prescribing" [Text Word] OR "Dosing error" [Text Word]) AND ("Renal impairment" [MeSH Terms] OR "Renal impairment" [Text Word] OR "Kidney diseases" [MeSH Terms] OR "Kidney diseases" [Text Word] OR "Renal function" [MeSH] OR "Renal function" [Text Word]) AND ("Africa" [Text Word]). AND/OR words were used for the identification of the articles. The search was conducted from 3 February to 3 March 2022, and all published articles available online until the day of data collection were considered.

Definitions used for this review

Renal impairment: Defined as having an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2. Studies, to be included, must determine the eGFR of patients via creatinine-based equations like the Cockcroft Gault (CG), the Modification of Diet in Renal Disease (MDRD), or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).[23,24]

Inappropriate drug dose adjustment/drug use practices: Prescribe medications at the incorrect dose/frequency and/or prescribe medications that are contraindicated based on the patient's renal function. This was evaluated based on noncompliance with guidelines or the summary of product characteristics/product information, or on the extent of medication elimination by the kidney, in which case medications were considered inappropriate if not adjusted in proportion to reduced renal clearance.[16,25]

Data extraction

The authors prepared a standardized data extraction form in Microsoft Excel. Key study characteristics were extracted, including the study area, author, publication year, study design, target population, sample size, inclusion criteria, study period, study setting, estimation of renal function, drugs used, the total number of prescriptions, total number of prescriptions with a drug that requires a dose adjustment, most common inappropriately used drugs concerning renal function, and factors associated with inappropriate dosing. Moreover, the outcome of interest, that is, prevalence of IDDA concerning renal function was also extracted. As a result, seven studies were selected based on their abstract, inclusion, and exclusion criteria.

Quality assessment

The Newcastle-OTTAWA quality assessment scale (adapted for cross-sectional investigations by Herzog et al.[26]) was used to assess the quality of selected studies. This quality rating tool is divided into three sections. The first section was concerned with the methodological quality of individual studies, which included objectives, sample size, and sampling methods. This section received a five-star rating. The second section of the instrument evaluated study comparability and assigned a two-star rating. The final section of the tool, which is graded out of three stars, evaluated outcome measurements and data analysis (Supplemental Tables A-1 to A-4). After summarizing the three components of the tool, studies with a 5-star rating or higher were included in the review and meta-analysis (Table 1).

Table 1. Quality assessment of encompassed studies in the review study.

Authors	Total quality (10 points)	Quality*
Decloedt et al.[27]	7	Moderate
Getachew et al.[28]	8.5	High
Gidey et al.[29]	6	Moderate
Dinsa et al.[30]	8.23	High
Sheikh et al.[31]	8.5	High
Zeleke et al.[32]	9.23	High
Obeid et al.[33]	8	High

*Scores from 0 to <6 have lower quality, $\geqslant$ 6–7 = moderate, and $\geqslant$7–10 considered high quality.

Outcome measures

The prevalence of IDDA for a renal function is the outcome measure in the present review and meta-analysis. It primarily aimed to assess the pooled estimates of inappropriate drug use/IDDA in the hospitals of Africa. A secondary outcome measure in this study was associated risk factors for IDDA practices in African hospitals.

Statistical analysis

We used Open Meta Analyst advanced software to analyze the pooled estimate of outcome measurements,[34] such as the prevalence of IDDA, prescriptions with a drug that needs a dose adjustment, as well as subgroup analysis. In addition, Review Manager version 5.4.1 software was utilized to assess the publication bias.[35] Egger's regression tests and funnel plots of standard error were utilized to assess and illustrate the presence of publication bias and small study size effects, respectively.[36] The precision was also demonstrated along with the Logit event rate. It was considered significant if a statistical test had a p-value of <0.05 (one-tailed).[37]

Heterogeneity assessment

In a systematic review and meta-analysis, heterogeneity can be considered as any form of variation between studies. The present study employed Der Simonian and Laird's random effects model considering the clinical heterogeneity between

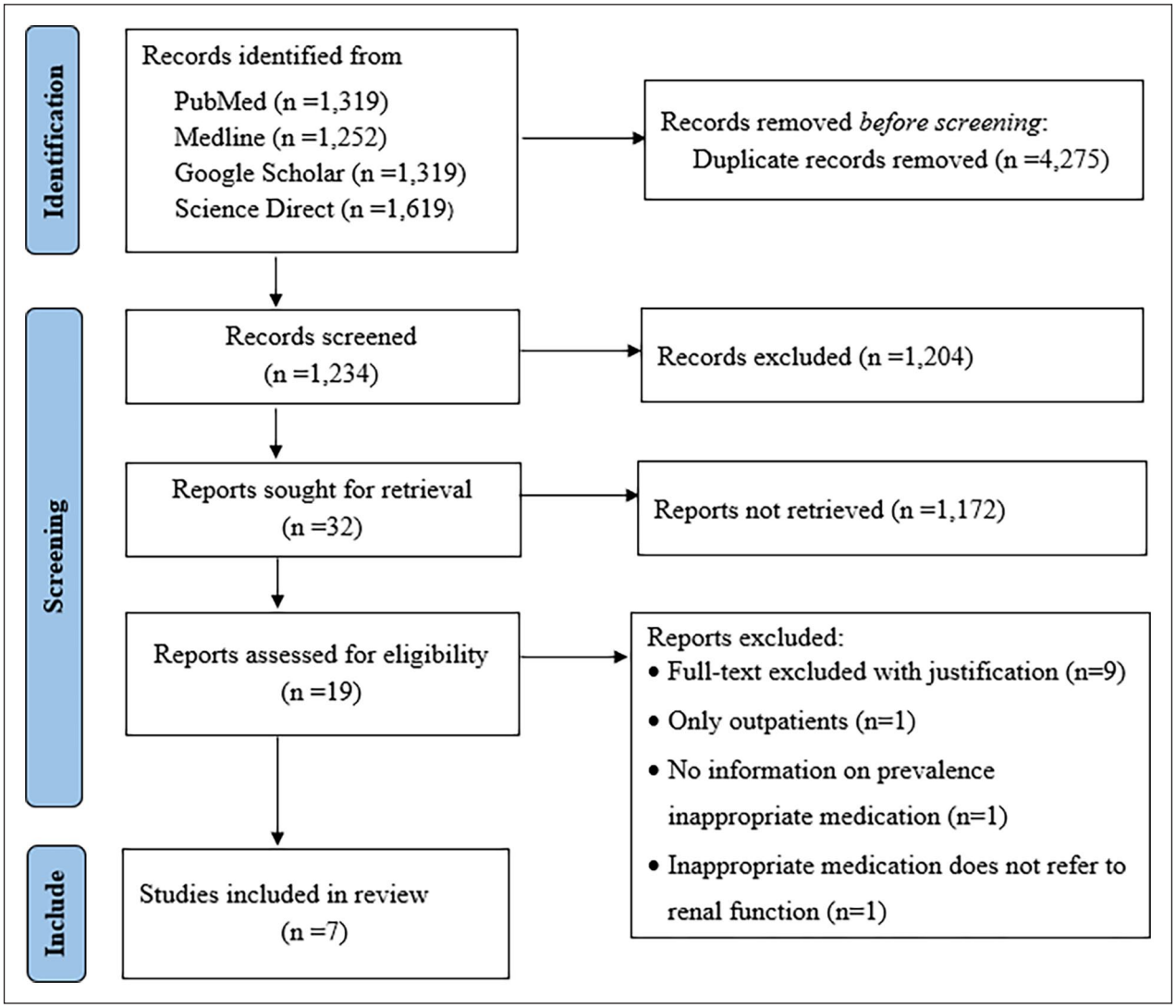

Figure 1. PRISMA flow diagram presenting the screening process.

studies. Clinical heterogeneity refers to the variation in patients, therapies, and outcomes evaluated. Methodological heterogeneity can be used to highlight study design variability and risk of bias.[38,39] This type of heterogenicity is frequently coming following the occurrence of either clinical or methodological heterogeneity or both across the included studies.[38] Cochran's Q-statistics, chi-squared, and I^2 tests are utilized to examine statistical heterogeneity. In the present review and meta-analysis, the clinical heterogeneity of included studies was measured using I^2 statistics. Based on the scores of the statistical test, I^2 statistics values of $<25\%$, from 50% to 75%, and $>75\%$ were considered as low, medium, and high heterogeneity, respectively.[40] The subgroup analysis was computed based on the sample size geographical location of the country in Africa.

We performed a sensitivity analysis to evaluate dominant studies and the change in the degree of heterogeneity and to verify the robustness of the study conclusion.[41] The stated odds ratio (OR) by 95% confidence interval (CI) and *p*-value were used to evaluate the correlates of IDDA.

Results

A full-text review of 19 potential publications was conducted after removing duplicates from a total of 1204 first hits. As a result, a total of seven papers met the review's inclusion criteria (Figure 1). Interestingly, the studies that were excluded during the extraction procedure were cited in the papers that were included in the analysis. Supplemental Table A-5 and Table 2 summarize the baseline characteristics, methods, and findings of the included papers, respectively.

Study characteristics

Ethiopian studies accounted for the majority of the included studies for the analysis ($n=4$; 57%). Botswana, Sudan, and

Table 2. Methods and results of the included studies based on inpatient data from the study setting.

Authors (year)	Estimation of renal function	Renal function in study population	Included drugs	Total number of prescriptions	Total number of prescriptions with a drug that needs a dose adjustment, *N* (%)	Prevalence of IDDA, *N* (%)	Most common IDDA drugs, *N* (%)
Decloedt et al.[27]	MDRD equation used to calculate eGFR	Median eGFR: 19 ml/min/1.73 m^2; median Cr: 448 µmol/l	No restrictions	615	117 (19%)	41 (34%)	Co-amoxiclavulanic acid, ciprofloxacin, and digoxin (five cases)
Getachew et al.[28]	eCrCl estimated by CG equation	Mean SCr: 2.24 ml/min; mean eCrCl: 39.6 ml/min	No restrictions	372	115 (31%)	58 (58%)	Cimetidine: 15/18 (83.3%); spironolactone: 2/16 (12.5%); vancomycin:10/14 (71.4%); ceftazidime: 7/11 (63.6%)
Gidey et al.[29]	MDRD equation used to calculate GFR	SCr: 3.94 mg/dl; CrCl: 28.84 ml/min	No restrictions	849	361 (42.5%)	168 (46.6%)	Ciprofloxacin (16 times), metoclopramide (15 times), and diclofenac (14 times)
Dinsa et al.[30]	eGFR was calculated using the CG, MDRD, and the CKD-EPI	Mean eGFR: 30.9 ml/min	No restrictions	422	163 (38.6%)	59 (35.6%) according to MDRD equation and 69 (42.3%) according to the CG equation	Not specified
Sheikh et al.[31]	MDRD equation used to calculate GFR	Mean SCr: 462.8 ml/min; mean eGFR: 29.3 ml/min/1.73 m^2	No restrictions	1143	234 (20.5%)	127 (54.3%)	Not specified
Zeleke et al.[32]	eGFR was calculated using CG equation	Mean eGFR: 32.71 ml/min/1.73 m^2	No restrictions	1581	815 (51.5%)	398 (48.8%)	63 (70.7%) followed by atenolol, ciprofloxacin, and ceftazidime
Obeid et al.[33]	eCrCl estimated by CG equation	No information	Cefepime	90	74 (82.3%)	71 (95.9%)	—

eCrCl: estimated creatinine clearance; CG: Cockcroft-Gault; eGFR: estimated glomerular filtration rate; MDRD: Modification of Diet in Renal Disease; SCr: serum creatinine; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; IDDA: inappropriate drug dose adjustment; PPIs: proton pump inhibitors; CrCl: creatinine clearance.

South Africa split the remaining 43% equally. The articles in this study were published between 2015 and 2021. These studies collected data between 2008 and 2019. All of the included articles were observational studies. One study was a prospective study,[28] while the other six were retrospective cross-sectional studies. The population sample in the included studies ranged from 73 to 422 patients (Supplemental Table A-5).

Patient characteristics

The inclusion and exclusion criteria such as age, hospitalization status, stated diagnosis, or CrCl were demonstrated in seven studies (Supplemental Table A-5). The majority ($N=4$) had imposed an age limit on study participants.[28,29,31,32] While the remaining three are barely referred to as adults in general.[27,30,33] One study included only chronic kidney disease (CKD) patients,[38] while the others included patients with acute kideny injury (AKI) or CKDs. The participants in those studies ranged in age from 42 to 54.6 years. Female patients made up 41%–55.6% of the total sample analyzed.

A couple of the three studies solely used the MDRD equation,[27,29,31] and CG equation,[28,32,33] to calculate the renal function. However, one article utilized CG, MDRD, and CKD-EPI equations.[30] The estimated GFR ranged from 19 to 39.6 ml/min on average across the studies reviewed. Using the MDRD and CG equations, the prevalence of estimated GFR 60 ml/min was 35.6% and 42.3%, respectively.

Quality assessment and score of included studies

As shown in Table 1, the quality scores of the included studies ranged from 6 to 9.23 on the Newcastle-OTTAWA grading scale.

Outcome measures

Based on total prescribed encounters, the pooled prevalence of IDDA among patients with renal impairment in Africa was 13.7% (CI = 7.9–19.5) (Figure 2(a)). The pooled IDDA rate was 39.3% (CI = 24.1–54.4) based on prescriptions with drugs requiring dose adjustments (Figure 2(b)). The pooled prevalence of IDDA revealed a significant heterogeneity ($I^2=97.25$, $p=0.001$) and ($I^2=98.01$, $p=0.001$); based on the reported total issued prescriptions and on prescriptions with drugs requiring dose adjustments, respectively.

The practice of inappropriate drug use in renal impairment

Six of the studies did not place any restrictions on the medications that might be used in their research, while the other study only looked at cefepime[33] (Table 2). Recommendations for dosage adjustments or probable contraindications in renal impairment were gathered from a variety of sources, including databases,[30] drug dictionaries,[33] and guidelines.[27–32]

Six of the studies focused solely on inpatient settings, while the other one looked at both inpatient and outpatient settings.[33] The total number of prescriptions analyzed varies between 90 and 1581.[32,33] On the other hand, the number of prescriptions containing at least one drug requiring dose adjustment ranges from 815 to 74.[32,33] Moreover, the prevalence of IDDA ranged from 34% to 95%.[30,33] Two studies reported inappropriate dosage and contraindications separately.[29,30] In these studies, dosing errors were more prevalent than in prescribing contraindicated medicine.

Generally, the most commonly reported medications with the usage of an unadjusted dose regimen were antibiotics, antidiuretics, protein pump inhibitors, histamine H2 antagonists, and antiarrhythmics. Consequently, the most frequently identified individual drugs associated with the usage of inappropriate use were ciprofloxacin ($n=3$), cimetidine ($n=2$), and spironolactone ($n=2$).

Factors associated with inappropriate drug use in renal impairment

As shown in Table 3, except for Gidey et al.,[29] all included studies used a univariate and multivariate regression model to identify the variable associated with inappropriate dose adjustment. However, only four articles revealed a statistical significance between the dependent variable and covariates.[28,30–32]

The common factors that predicted drug dose adjustment were the number/types of prescribed medicines. Thus, a total of three studies also indicated the association between drug adjustment and the number of medicines prescribed.[28,31,32] Additionally, one study also indicated a type of prescribed medication as a predictor.[28] Two studies used the number of drugs per prescription considered as a continuous variable,[28,32] while the other used it as a categorical variable.[31] All articles that reported polypharmacy as a predictor were concise in reporting that the higher the polypharmacy rate, the higher the risk for IDDA among renally impaired patients.

Age, stage of renal impairment, comorbidity, and unemployment were also reported as predictors in Getachew et al.,[28] Dinsa et al.,[30] and Zeleke et al..[32] Even though six studies considered age through categorical variables, only one study revealed increasing age emerged as a risk factor for affecting drug dose adjustment practice. In one study, stage 4 renal impairment was found to be a predictor of dosing errors, with an OR of 587.7.[28] Zeleke et al.[32] reported the number of comorbidities and unemployment was predicator with OR = 1.65 and 3.18, respectively. Additionally, one study used a clinical outcome as a dependent variable and IDDA as an independent variable.[33] As a result, the regression model in the study revealed a significant association between high sCr and inappropriate drug usage.

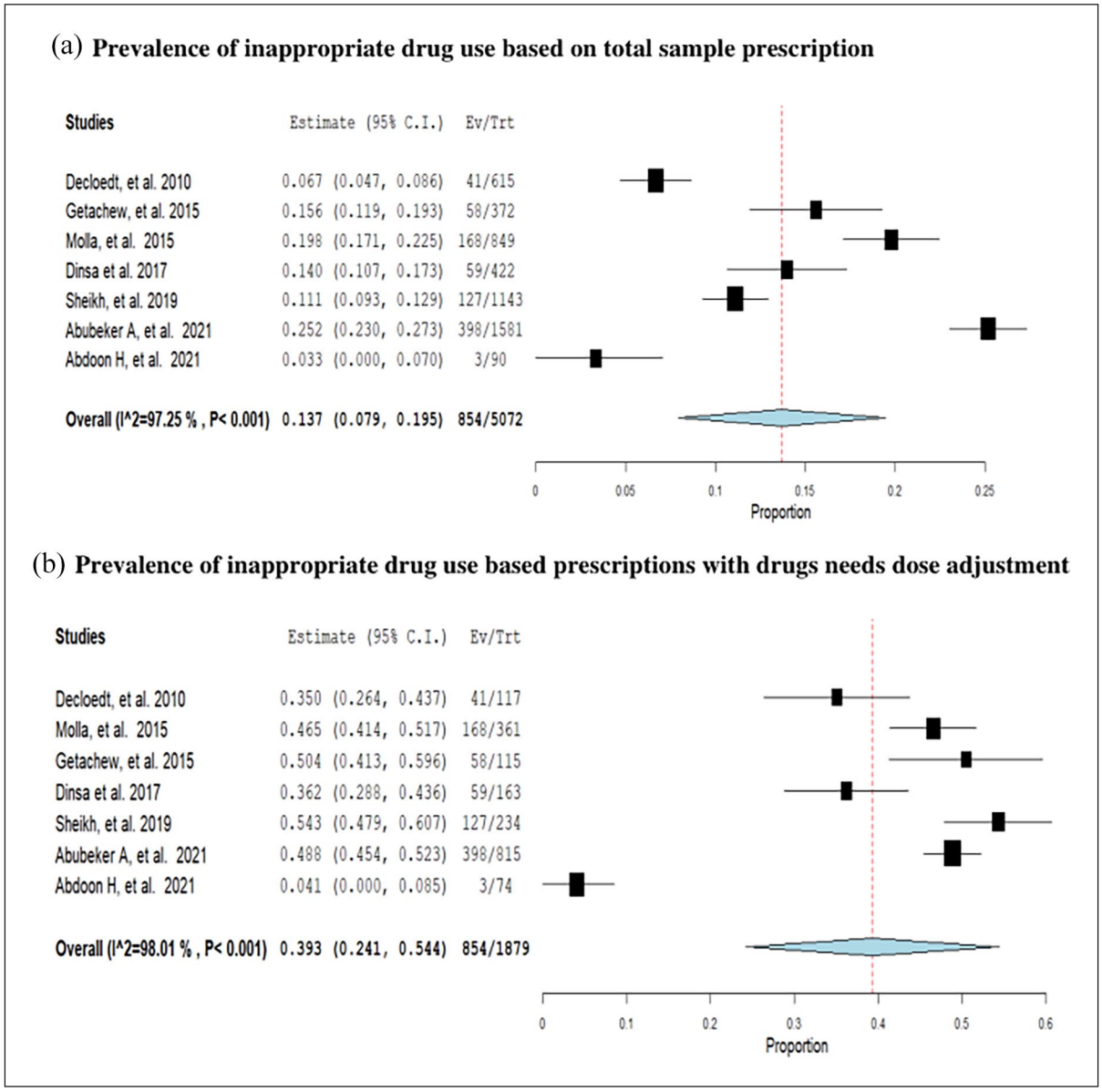

Figure 2. The pooled prevalence of inappropriate drug use drugs among adult patients with renal impairment in Africa: (a) prevalence of inappropriate drug use based on total sample prescription and (b) prevalence of inappropriate drug use based prescriptions with drugs needs dose adjustment.

Table 3. Predictors of inappropriate drug use among adult patients with renal impairment in Africa.

Predicator	Description
Number/types of prescribed medicines	The higher number of drugs per prescription was a risk factor for IDDA.[31,32] Three or more prescriptions per encounter, the more likely that inappropriate dosage adjustments would be made.[31] The type of prescribed drug and IDDA were observed during multivariate regression analysis. Thus cimetidine, vancomycin, ceftazidime, and digoxin were less likely to be appropriately adjusted than other types of medicines.[28]
Stage of renal impairment	IDDA was associated with the stage of renal dysfunction.[28]
Age	Older than 70 years old is associated with the prevalence of inappropriate dose adjustment.[30]
Comorbidities and unemployment	Patients with comorbid conditions and unemployed were more likely exposed to IDDA.[32]

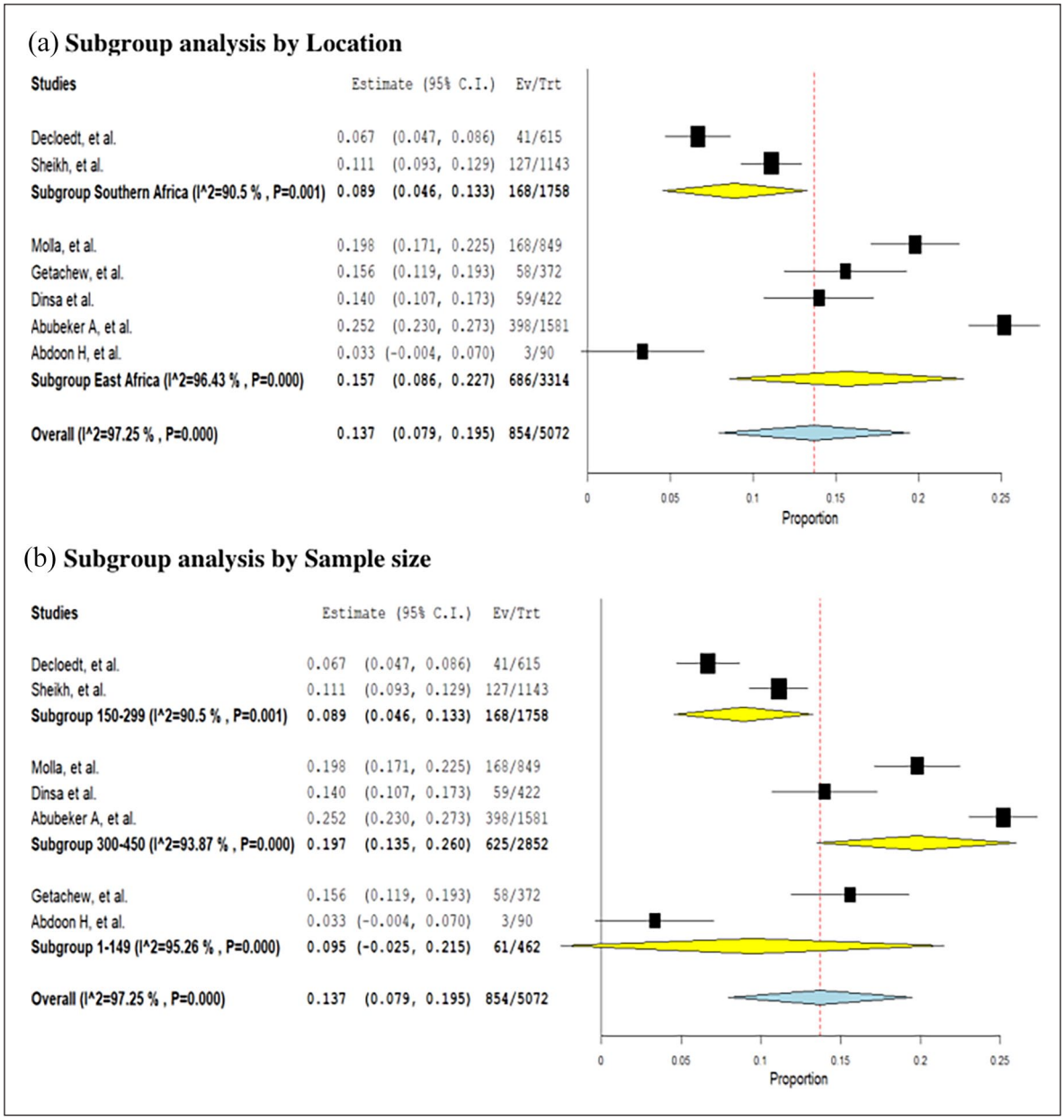

Figure 3. Subgroup analysis of the prevalence of inappropriate drug use based on location and sample size among adult patients with renal impairment in Africa: (a) subgroup analysis by location and (b) subgroup analysis by sample size.

Sensitivity analysis, subgroup analysis, and meta-regression

The leave-one-out sensitivity analysis demonstrated no variability in the degree of heterogeneity. Thus, the pooled prevalence of inappropriate drug use was laid in a range of estimated CI (Supplemental Figure A-1).

According to subgroup analysis based on geographical location, the pooled prevalence of inappropriate drug use was higher in eastern Africa. Similarly, subgroup analysis of studies with sample sizes between 300 and 450 showed a higher pooled prevalence of IDDA (Figure 3). According to a meta-regression analysis, a source of heterogeneity was the number of prescriptions containing medications that required dose adjustment ($p < 0$) (Figure 4).

Publication bias

There was no evidence of publication bias in the funnel plots of standard error with the logit effect size for the prevalence of IDDA practices. Figure 5, studies are clustered around the line, indicating that there is no publication bias.

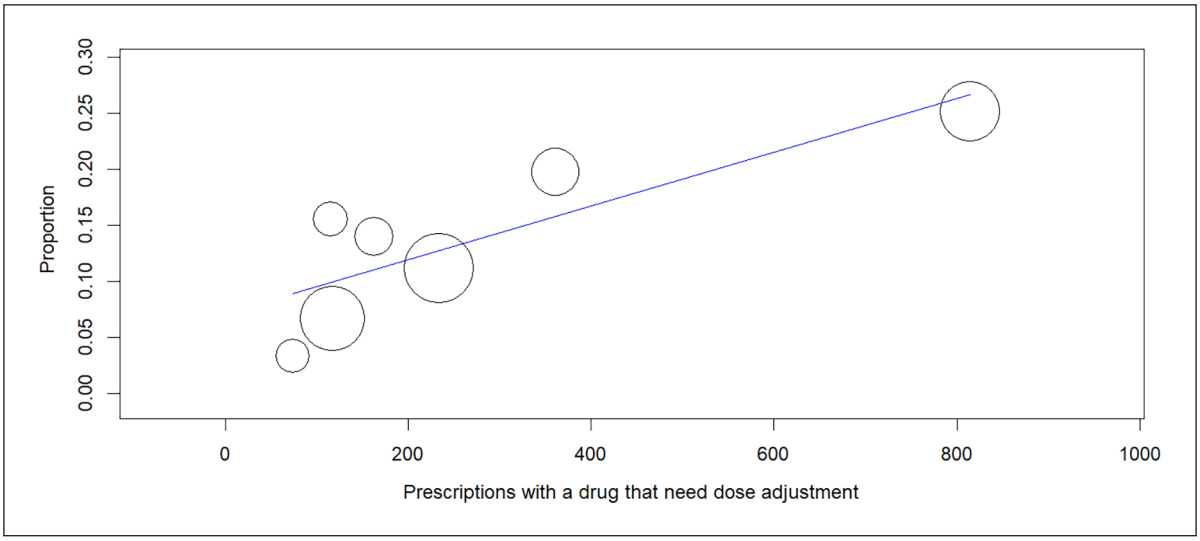

Figure 4. Univariate meta-regression model by the number of prescriptions containing drugs that need dose adjustment for the prevalence of inappropriate drug use in Africa.

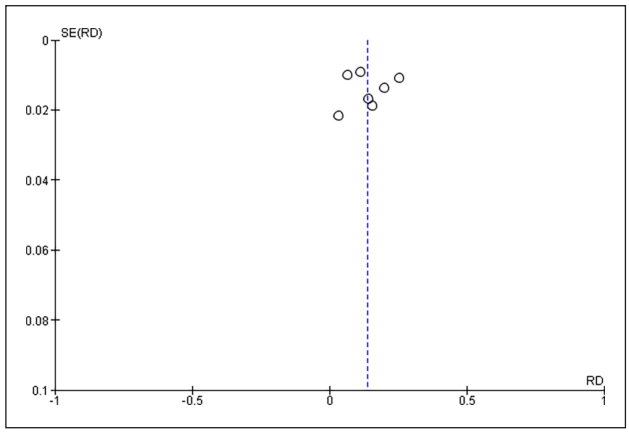

Figure 5. Funnel plot of the prevalence of inappropriate drug among adult patients with renal impairment in Africa.

Discussion

The present systematic review and meta-analysis have aimed to examine and quantitatively summarize the pieces of scientific literature in Africa; on the prevalence of IDDA and associated factors among inpatients with renal impairment. From all eligible studies, 1918 patients were included in the pooled estimation of the outcome measure. A total of 5072 prescriptions were reviewed and 1879 of them contained at least one drug that need a dose adjustment. This means that for every 2.7 prescriptions, at least one drug requires a dose adjustment (calculated by dividing the number of prescriptions and the number of encounters containing at least one drug that needs dose adjustment). In other words, at least one IDDA occurs for every two prescriptions containing a drug that required a dose adjustment (calculated by dividing the number of encounters containing at least one drug that needs dose adjustment by the number of IDDA).

The pooled prevalence of non-adjusted drug use among adult patients with renal impairment in Africa was revealed 13.7% (CI = 7.9–19.5). Based on the number of prescriptions with drugs that needs dose adjustment, the pooled prevalence of IDDA was 39.3% (CI = 24.1–54.4). This remarkable practice of IDDA was also reported in review papers by Tesfaye et al.[20] The study reviewed 49 papers from 23 countries and revealed the prevalence ranges from 9.4% to 81.1% among hospitalized CKD patients. A similar other review study published in 2017 also reported the prevalence of unadjusted drug use among outpatients ranges from 1% to 37%.[21] This could imply that a significant amount of inappropriate drug prescription and use among renal insufficient patients has persisted globally. Moreover, in this study, almost half of (932/1879) prescriptions containing drugs that need to be adjusted were administered without adjusting the dose relating to renal function. A possible explanation could be the lack of use of an automated report system of renal function with eGFR in African settings.[28] This reporting system helped the prescribers in developed countries to adjust the dose if needed by alerting them.[8,42] The other possible reason might be due to the high burden of kidney disease, but there is a shortage of overall healthcare providers, and a lack of awareness and training of prescribers regarding dose adjustment in health facilities in Africa.[28,43]

This study also identified the common factors affecting IDDA relating to renal function. These factors are the number/types of prescribed medicines (most common), age, stage of renal impairment, comorbidity, and unemployment. Several studies have also indicated the interdepends between these covariates. For example, it was revealed that increased

age, severe renal dysfunction, and comorbidity are associated with a higher number/types of prescribed medicine per patient.[20,43] Polypharmacy is not only associated with impaired renal function, but it is also a risk factor for inappropriate prescribing practices.[44] Concern should be expressed for elderly patients because age is associated with comorbidity (a risk factor for increased polypharmacy) and renal dysfunction.[44,45]

The findings of this study could provide stronger evidence on the extent of IDDA practices and associated factors, allowing healthcare professionals, policymakers, and researchers to be concerned and understand the situation, review and analyze the effectiveness of applying guidelines, and identify gaps and the need for additional research such as random clinical trials.

Literature comparisons

Compared to the reviews of Tesfaye et al.[20] and Dörks et al.,[21] the present study added meta-analysis and utilized a modified search strategy specific to African studies. As a result, the final number of included studies was lower than those reviews. In this review, the estimation of renal dysfunction showed variability due to differences in method, inclusion and exclusion criteria, and cut-off points (Supplemental Table A-5). Therefore, it was difficult to observe a clear trend across the study settings. Because six studies put no restrictions on the drug type, the clinical outcome of the studies cannot be compared due to differences in their denominator. Some studies estimated the prevalence of IDDA by sample size, the number of prescriptions, or both. So, we managed to use the number of prescriptions for estimating the pooled prevalence of inappropriate drug use. Furthermore, comparing reviews, this study has included both acute and chronic kidney patients. This could be advantageous to grab an overall image of the prevalence of inappropriate prescribing and usage of renal excreted medications. However, there is a limited study regarding drug dose adjustment trends in Africa.

The majority of the studies included in this study used the proportion of IDDA calculated by the CG equation. Several equations such as CG, MDRD, and CKD-EPI are commonly utilized to calculate GFR which is responsible for diverse results.[46–48] CG equation is the oldest and most commonly utilized equation but tends to underestimate the GFR (has higher results than others), particularly in elderly patients. However, recent equations such as MDRD and CKD-EPI are preferred nowadays due to their estimation based on sCr measured by recent assessment methods and attuned to the body surface. For example, in the study of Dinsa et al.[30] The prevalence of IDDA was 42.3% and 35.6% according to CG and MDRD equations, respectively. This could mean that the need for drug dose adjustment is determined by the choice of such equations. Therefore, this condition should be considered before prescribing medications for the risk group.[44,46]

Study limitation

MeSH terms and text words from titles and abstracts are used to find the relevant studies. As a result, research that may have satisfied the objectives of the study but used words other than those in the search strategy may have gone undetected. However, we have tried to use the maximum possible search keywords in the area of the topic. Another limitation is that because so few studies have been reviewed, determining the actual prevalence of IDDA may be difficult. Third, the pooled estimation of meta-analysis may be biased since only online articles were included in the analysis. The observed absence of publication bias may not be accurate due to the inclusion of a modest number of studies and some with small sample sizes. Additionally, because the meta-analysis included both CG and MDRD models, the pooled prevalence of IDDA may be overestimated or underestimated. Finally, because all of the included studies are observational studies, this review and meta-analysis are unable to assess how using an inappropriate dose may affect patients.

Conclusion

The pooled prevalence of inappropriate drug use among adult patients with renal impairment in Africa was revealed 13.7% (CI = 7.9–19.5). The pooled prevalence of prescriptions containing drugs that require a dose adjustment is estimated to be 39.3% (CI = 24.1–54.4). In the present review, the number/types of prescribed medicines, age, stage of renal impairment, comorbidity, and unemployment were identified as a factor for inappropriate prescribing and usage.

According to our findings, inappropriate drug dose prescribing and practice seems to be a common challenge among inpatients in Africa. However, generalizability is a challenge for any final suggestions because there was variation in GFR calculation, cut points, and types of drugs evaluated across included studies. Furthermore, findings from observational research must be supported by outcome studies to examine patient-related outcomes of incorrect dosage utilization and prevent its prescribing. A few published works from African countries were retrieved for this study. Much more research (from each nation) is needed on the area of study in an African context.

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Author contributions

DD conceived the idea of the topic. DD and GA designed the study. GA and TE collected relevant investigations, evaluated the study quality, and extracted and analyzed the data. DD and ZB commented on the review and meta-analysis. GA also prepared the manuscript for publication. All authors have read and approved the manuscript.

Availability of data and materials

All data included in this review has been cited and can be accessed online.

Declaration of conflicting interests

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Supplemental material

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