Systematic Review

Prevalence of Diabetes Mellitus among individuals with chronic kidney disease: systematic review and meta-analysis

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ABSTRACT | INTRODUCTION: Diabetes Mellitus (DM) is currently considered a global epidemic, with alarming estimates for the coming years on all continents, with Chronic Kidney Disease (CKD) as one of its main consequences when a timely diagnosis is not made. **OBJECTIVE**: The objective of this study is to estimate the prevalence of DM among individuals diagnosed with CKD by means of a systematic review and meta-analysis. **METHODS:** A systematic review was carried out in the main free-access databases such as Pubmed (Medlaine), Lilacs, Scopus and Scielo. Two researchers selected the articles, extracted the data and evaluated the quality. The collected data were evaluated using a random effects model. **RESULTS:** Of 994 articles, 17 studies were included that looked at three continents. The group prevalence of DM among individuals with CKD (95% CI) was 29% (23-35%), with heterogeneity I^2 = 99,86% and p = 0.00, which was not explained by meta-regression and subgroups. **CONCLUSIONS:** The present study confirmed the high prevalence of DM among individuals with CKD, especially among those with end-stage renal disease, demonstrating the need for early diagnosis and timely treatment of DM and new studies in this area, considering the social and economic impact of these diseases worldwide.

KEYWORDS: Diabetes Mellitus. Chronic kidney disease. Systematic review. Meta-analysis. Prevalence.

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Background

Diabetes Mellitus (DM) is closely associated with Chronic Kidney Disease (CKD), both of which are considered to have a major impact on global public health, due to their health, human, social and economic implications. Those individuals who are not diagnosed in a timely manner are at greater risk of developing macro and microvascular complications, including cardiovascular disease, stroke, limb amputations and CKD.[1]

The International Diabetes Federation (IDF), which published a study indicating the estimated prevalence of worldwide DM for the years 2017 and 2045, indicated a projection of 425 and 629 million people with the disease in the age group of 20-79 years, respectively. Moreover, this increase will occur mainly in regions of low and middle-income economies, with more than one-third of the diabetes cases resulting from population growth and aging.[2]

Given this scenario, the increase in the incidence of diabetic renal disease (DRD) is sustained by a global imbalance between overnutrition and physical inactivity, leading to excess weight and obesity. Between 2005 and 2015, the prevalence of DRD increased by 39.5% globally and mortality increased by 31.7% in the last 10 years, mainly in Latin America and in low and middle-income countries, which surely burdens the health systems due to expensive kidney replacement treatments.[3,4]

Updates to DM prevalence data among individuals with CKD are of great importance for the elaboration of public health actions, since these individuals have greater and more complex care needs, which leads to more expenses, besides raising the rates of morbidity and mortality in relation to non-diabetic individuals.[5,6]

Given the magnitude of this problem, the objective of the present study is to estimate, through a systematic review and meta-analysis, the prevalence of DM among individuals diagnosed with CKD.

Methods

This study was carried out based on the recommendations proposed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA)[7] guide consisting of a checklist presenting 27 items and a flow chart, with the objective of analyzing the scientific production on the prevalence of DM among CKD patients worldwide.

Protocol and Registration

The protocol of this systematic review was recorded in the International Prospective Register of Systematic Reviews (PROSPERO) under the number CRD42018095911.

Eligibility criteria

Cross-sectional and cohort studies that met the proposed goal and described the prevalence of Type 1 DM and Type 2 DM in individuals with a diagnosis of CKD were considered eligible. To be included, the studies needed to meet the following criteria: they were original studies and reported the prevalence of DM in individuals ≥ 10 years with a diagnosis of CKD, in use of hypoglycemic and insulin medications or diagnosed by fasting glycemia (≥ 126 ml/dl) or by glycated hemoglobin (≥ 6.5%). The CKD should be confirmed by the presence of a glomerular filtration rate (GFR) <60 ml/min /1.73 m2 and/or albuminuria ≥ 30 mg/g and dialysis treatment in reference centers and hospitals. Exclusion criteria were: review studies, studies on the prevalence of gestational diabetes mellitus, and case series, case control and duplicity studies.

Sources of information and research strategies

The article search was carried out in May of 2020 and systematized in the following databases: Medline (via Pubmed) and Scopus, Latin American and Caribbean Literature in Health Sciences (Lilacs) and Scientific Electronic Library Online (SciELO).

In the search strategies, the following descriptors (search terms) were used: “diabetes mellitus”, “chronic kidney disease”, “prevalence”, “frequency”, “incidence”, “medical research”, “obesity”, “cardiovascular disease”, “research article”, and “medicine” according to DeCS/ MeSH and with the Boolean operators “AND” and “NOT”, adapted for each scientific database. The bibliographic search was performed until May 2020 and was restricted to 3 languages, being: English, Spanish and Portuguese.

Selection of studies and data extraction

According to the eligibility criteria, the authors independently selected the studies in two stages, evaluating the title and abstract, and later reading the full text. Disagreements were resolved by consensus.

In order to extract the data, a spreadsheet was prepared in which information was registered about the following: name of the study, authors, year of data collection, continent, city, country, objective, age group, the existence of previous sample calculation, type and size of the sample, incidence and prevalence of DM, incidence and prevalence of CKD and diagnostic method used.

The articles that weren't possible to obtain on the available scientific bases were requested from the interlibrary exchange service, Interlibrary Bibliographic Exchange (COMUT), maintained by the Brazilian Institute of Scientific Information (IBICT).

In order to assist in the planning, execution and summarization of the data, the State of the Art through Systematic Review (START) software version 3.0.3 Beta and the Mendeley software for reference management were used.

Evaluation of the methodological quality of included studies

To determine the quality of the articles, the instrument for critical evaluation of prevalence studies proposed by Loney et al (1998)[8] was used, with adaptations. Eight criteria were adopted by the authors: 1) probabilistic or census sampling; 2) adequate sampling source; 3) sample size (> 300); 4) diagnostic methods (according to the inclusion criteria); 5) impartial assessment by trained evaluators; 6) adequate response rate (> 70.0%) and description of refusals; 7) presentation of confidence intervals and analysis of subgroups of interest; and 8) study subjects well described and similar to the research question.

For each criterion met, the study received one point. High-quality studies were those with scores of 7 and 8; moderate quality, 4 to 6 points; and low quality, 0 to 3 points. It should be noted that the evaluation of quality was not used as a criterion for the exclusion of articles, being a parameter for heterogeneity study and subgroup analysis.

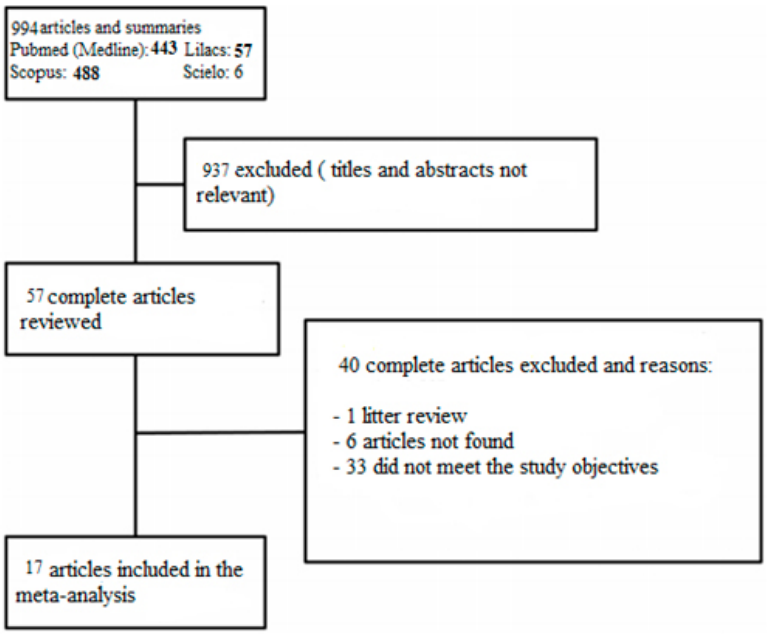
Data Analysis

The primary endpoint was the prevalence of DM among individuals with CKD at all stages of the disease, with a 95% confidence interval (95% CI) and a significance level of 5%. The summary averages were estimated for the general population and subgroups defined as the year of collection, year of publication, design, sample size, quality of study, continent, and place of data collection. The meta-analyzes and meta-regressions were calculated with the objective of identifying the causes of heterogeneity and also to evaluate the existence of the small-study effect, by means of visual inspection of the funnel graph and the Egger test[9] calculation. The analyzes will be performed with the "Metaprop" and "Metareg" command of the Statistics / Data Analysis (Stata) software, version 11.2.

Results

The search resulted in 994 articles and after the duplicates were removed, the titles and abstracts were evaluated for relevance, leaving 57 articles for complete analysis. The extraction and evaluation of detailed data were conducted in 17 articles according to Figure 1. No additional studies were identified by examining reference lists.

Figure 1. Flowchart of search results, selection and inclusion of eligible studies



Source: The authors (2023).

Figure 1 outlines the selection stages of the articles and the final number of those eligible for the systematic review and meta-analysis, as well as the number and justification of excluded articles. Data were collected from the authors of 17 studies.[10-26]

Amongst the included articles, the data collection was carried out between 1985 and 2018, with 57.1% of the studies being published before 2004. Regarding the place of study, Latin America and Central America had a higher number of studies[10-12,14-21,25,26] (82,4%%), Asia[20,22] (11,7%) and Europe[13] (5,88%), with a predominance of studies carried out in Brazil[10-12,16-18,24] (41,17%). Most of the studies were carried out in Hemodialysis Centers [10,12,14-17,20-22,24-26] (58,8%), and cross-sectional studies were included[11,12,15,17,18-20,22] (64,7%) and longitudinal[10,13,14,16,21,23] (42,9%).

The sample size ranged from 45 to 57755 participants per study. A total of 113.013 individuals were investigated, with the Takaoka et al. (2009)[11] study presenting the lowest number of participants (n = 97) and the study of Diaz (2018) carried out in Cuba.[25] As for the age group of the individuals in the studies these include from childhood to the elderly, with mostly adults and elderly (Table 1). Regarding the methodological quality of the studies[8] 76,5% presented moderate quality and 23,5% were classified as high quality. No study presented poor quality (Table 1).

Table 1. Epidemiological characterization of included studies on Prevalence of Diabetes Mellitus among individuals with Chronic Renal Disease (to be continued)

Name of Study	Year of Research	Country / Continent	Collection Location	Kind of study	Sample (n)	Prevalence DM (%)	Age group (Years)	Sex (%)	Punctuation
Bersan, et al (2013)	2004 a 2008	Brazil South America	Hemodialysis centers	Longitudinal Study	311	47,2	± 62	55,5% M 44,5% F	7
Takaoka, et al (2009)	2006	Brazil South America	Hospital	Cross-Sectional Study	97	16,5	± 58	54% M 46% F	5
Burmeister, et al (2012)	2009	Brazil South America	Hemodialysis centers	Cross-SectionalStudy	1288	**37,8**	-	-	6
Kolenysk, et al (2014)	2010 a 2012	Ukraine Europe	Nephrology Centers	Longitudinal Study	5985	20	45-65	55% F 45% M	6
Mungrue, et al (2011)	2002 a 2007	Venezuela South America	Hemodialysis centers	Songitudinal Study	107	31,7	10 -79	52% M 48% F	5
Cieza,et al (1992)	1990	Peru South America	Nephrology Centers, Hemodialysis centers, Hospital	Cross-SectionalStudy	734	10,9	10 a > de 80	56% M 44% F	6
Peres, et al (2007)	1985 a 2005	Brazil South America	Hemodialysis centers	Longitudinal Study	645	47,1	-	60,3% M 39,7% F	5
Beirys, et al (2009)	2006	Cuba Central America	Hemodialysis centers	Cross-Sectional Study	45	51,1	18 -80	48,58% M 51,42% F	5
Rodrigues, et al (2010)	1988 a 2008	Brazil South America	Individuals with DM1 attended at outpatient clinic	Cross-Sectional Study	573	24	≥16	50,5% M 49,5% F	8
Ronqui, et al (2007)	2004	Brazil South America	Laboratory of Nephrology	Cross-Sectional Study	114	47,3	>11	36,9% M 63,1% F	5

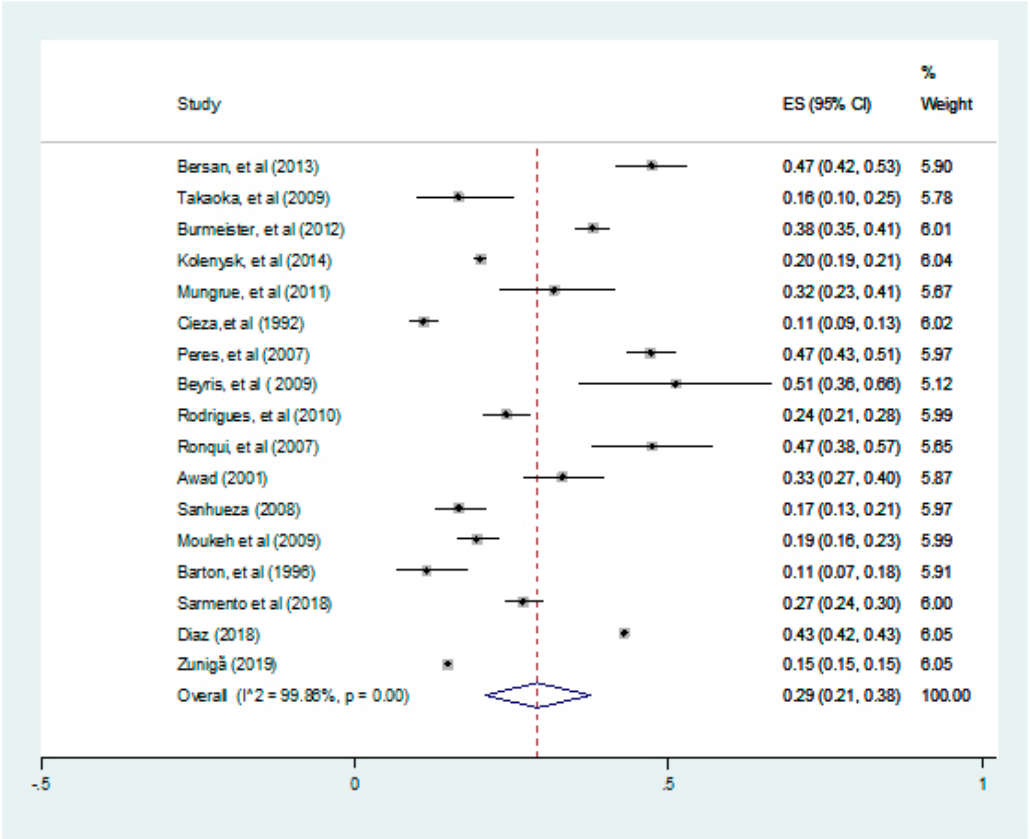
Table 1. Epidemiological characterization of included studies on Prevalence of Diabetes Mellitus among individuals with Chronic Renal Disease (conclusion)

Name of Study	Year of Research	Country / Continent	Collection Location	Kind of study	Sample (n)	Prevalence DM (%)	Age group (Years)	Sex (%)	Punctuation
Awad (2001)	2008 a 2009	Iraq Asia	Hemodialysis centers	Cross-Sectional Study	230	33	7 - 108	53% M 47% F	7
Sanhueza (2008)	1999	Chile South America	Hemodialysis centers	Longitudinal Study	57	16,5	57 - 62	52,6% M 47,4% F	5
Moukehet al (2009)	2006	Syria Asia	Hemodialysis centers	Cross-Sectional Study	550	19,5	5 - 82	50,9% M 49,1% F	5
Barton, et al (1996)	1993	Jamaica Central America	Hospital	Longitudinal Study	140	11,4	12-87	55,5% M 45,5% F	5
Sarmento et al (2018)	2016	Brazil South America	Hemodialysis centers	Cross-Sectional Study	818	26,7	± 55,7	-	6
Diaz (2018)	2018	Cuba Central America	Outpatient clinc	Cross-Sectional Study	57755	42,9	19-65	50,3% M 49,7% F	5
Zunigã (2019)	2013	Peru South America	Outpatient clinic	Cross-Sectional Study	42746	14,8	± 69,2	41,8% M 58,2% F	7

Source: The authors (2023).

The pooled prevalence of DM among individuals with CKD (95% CI) was 29% (23-35%), and the studies showed high heterogeneity I^2 = 99,86% and p = 0.00 (Figure 2). After carrying out univariate meta-regression, none of the explanatory variables analyzed were able to explain the causes of the heterogeneity found in the analysis between the studies.

Figure 2. Forest plot of prevalence of Diabetes Mellitus among Individuals with Chronic Kidney Disease



Source: The authors (2023).

The visual inspection of the funnel chart revealed asymmetry in the distribution of the studies, but the effect of small studies was ruled out by Egger's test (p = 0,249).

Discussion

From the results obtained in the analyzed articles, a considerable prevalence of DM (29%) among the CKD patients is estimated, demonstrating the importance of carrying out further studies on this subject.

South and Central America presented the highest prevalence while Europe was the continent that presented the lowest prevalence.

It is known that DM is a global disease emergency of great magnitude with potential quality of life loss leading to individuals' disability, besides causing enormous social and economic impact in several countries due to its severe complications, especially with CKD. This association was found in a study conducted in the UK adult population in 2011, which demonstrated that one-fifth of individuals with DM will have CKD, making diabetes the most common cause of advanced stage renal disease.[23]

In a study carried out in Brazil[12], the prevalence of DM found among individuals with CKD was 37.9%, a percentage higher than the result of the prevalence found in this systematic review. The author attributed this finding mainly to the following reasons: the decrease in mortality among diabetic patients on hemodialysis, a fact that has already been observed in other countries[27], the presence of elderly individuals with DM (due to prolonged life expectancy)[28] and the increase in obesity in the general population.[29]

The prevalence of DM found in a study amongst five populations from three regions of Venezuela was 8.3%.[27] Although this percentage was lower than the prevalence found in the present study (29%), it was reported that less than half (48.2%) of the individuals with DM had knowledge that they had the disease, which shows a fragility in the healthcare system to establish effective policies to provide care for this population group. It should be noted that the countries of South America are where the most studies on the prevalence of DM among individuals with CKD have been published.

A population-based survey conducted in Canada in 2013 (Canadian Health Measures Survey) found a DM prevalence of 10.9% among individuals with CKD. A similar result was observed in Tanzania, an African country whose prevalence was 12.1%.[30]

High heterogeneity was found in the analysis of the results and could not be explained by the subgroup analysis and meta-regression. This heterogeneity can be explained by clinical and methodological variability. Clinical variability (variability among participants) may be due to the natural differences between the individuals included in the studies, considering how each country has its own unique characteristics from the perspective of socioeconomic, cultural and disease profiles. Regarding methodological variability, we observed some studies with small sample sizes and different diagnostic methods for CKD and DM, as well as different inclusion criteria and study longevity which may have led to these differences between them. In addition, a small number of studies, which were included following Prisma's methodological criteria, can explain the heterogeneity.

It is noteworthy that the present study confirms DM as an important risk factor in the development of CKD and end-stage renal disease. This systematic review and meta-analysis is significantly innovative, as no other review studies on this subject were found according to PROSPERO. It is also worth noting the absence of articles of low quality and publication bias.

The limitations found in the study are the following: high heterogeneity and the fact that no study met all quality criteria. In addition, the Loney scale, generally used for prevalence studies, presents as a limitation the attribution of equal weights to each evaluated item. In general, the use of scales for quantitative evaluation allows the scores to be used as a weighting factor in the statistical analysis of the results of a meta-analysis, giving greater weight to studies of better quality.

The findings of this systematic review and meta-analysis confirmed the high prevalence of DM among individuals with CKD, showing that DM is an important global health problem and if not diagnosed in a timely manner is directly associated with CKD and ESRD, generating high human costs and economic resources, especially RRS. It is recommended to carry out new studies that evaluate strategies of DM intervention in order to intervene in the progression of CKD, highlighting the need for studies in the African continent and North America. It is also recommended that studies should be performed on DM prevalence among individuals diagnosed with CKD that address diagnostic criteria and demographic data on the population, as well as unadjusted and adjusted findings.

List of abbreviations

DM: Diabetes Mellitus
CKD Chronic Kidney disease
IDF: International Diabetes Federation
DRD: Diabetic Renal Disease
PRISMA: Prefered Reporting Items for Systematic Reviews
IBICT: Brazilian Institute of Scientific Information
START: State of the Artthrough Systematic Review

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Author's contribution

Borges LD, Dias HH, Alves PM, Silva BO, Santos KP, Costa GD, Santos DS designed the study, analyzed the data, interpreted the study results, and wrote the manuscript. Ferreira ES, Moreira TR and Cotta RMM supervised the data analysis, contributed to the writing and revision of the manuscript and approved the final manuscript for submission. All authors read and approved the final manuscript.

Conflicts of interest

No financial, legal or political conflicts involving third parties (government, corporations and private foundations, etc.) have been declared for any aspect of the submitted work (including, but not limited to grants and funding, advisory board participation, study design, preparation of manuscript, statistical analysis, etc.).

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