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CHRONIC KIDNEY DISEASE OF UNCERTAIN ETIOLOGY: A SYSTEMATIC REVIEW

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Absract

Background: *CKD is a global health issue. Its frequency is 11%–13%. Even though figures aren't available, cases are rising in high-income, low-income, and middle-income countries.3 Most countries' chronic kidney disease (CKD) is caused by diabetes and high blood pressure. Some countries have "nontraditional" CKD causes that are unknown.*
The Aim: *this study want explore about chronic kidney disease (CKD) of uncertain etiology.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 27 articles, whereas the results of our search on SagePub brought up 19 articles. The results of the search conducted for the last year of 2013 yielded a total 8 articles for PubMed and 4 articles for SagePub. In the end, we compiled a total of 11 papers, 9 of which came from PubMed and 2 of which came from SagePub. We included three research that met the criteria.*

Conclusion: *There are several reasons a person can experience CKDu, for example physical conditions such as heat and chemical components such as arsenic.*

Keyword: *Chemical compound; Chronic kidney disease; Heat; Occupation*

INTRODUCTION

Chronic kidney disease (CKD) is a term used to indicate a decrease in kidney function caused by mild, moderate, or severe chronic kidney damage. Chronic kidney disease is a public health problem worldwide. The increasing incidence and prevalence of CKD, with poor outcomes and high costs, has occurred in many countries.[1] The normal kidney contains about 1 million nephrons which contribute to the total glomerular filtration rate (GFR). The kidney has an innate ability to maintain GFR in the face of kidney attack (regardless of etiology), although nephron destruction is progressive. The remaining healthy nephrons undergo compensatory hyperfiltration and hypertrophy.[2]

Chronic kidney disease (CKD) is a growing public health problem that affects people all over the world. Its frequency is said to be between 11% and 13%. The number of cases is going up not only in high-income countries, but also in low-income and middle-income countries, even though exact numbers aren't known from these places.[3] In most countries, diabetes mellitus and high blood pressure are the two most common causes of chronic kidney disease (CKD). In some countries, there are also "nontraditional" reasons of CKD that are not well understood.[4–6]

The disease progresses with few or no symptoms until it has reached an advanced stage. Some of the markers that can detect CKD in its earliest stages are difficult to obtain. Before clinically apparent proteinuria/albuminuria or a decline in glomerular filtration rate (GFR), the majority of early manifestations of CKDu are associated with tubular abnormalities and changes in urinary detritus. There are additional difficulties in accurately estimating GFR, and by the time there is a definite decline in estimated GFR, the disease will be obviously advanced and irreversible. These are some difficulties in diagnosing CKDu.[7]

Several diseases and condition can cause glomerular disorders.[1,2] In the meantime that the international community is rallying support to combat the epidemic of CKD in urban populations, CKD of unknown aetiology (CKDu) is being increasingly reported from isolated, primarily rural settings in different regions all over the world. In particular, cases of CKDu have been documented in Nicaragua, El Salvador, Costa Rica, Sri Lanka, India, Tunisia, and Egypt.[4–6,8–10] The chronic kidney disease (CKD) of unknown aetiology is the focus of this research project, the purpose of which is to learn more about the condition.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

In this literature review, we investigate the various alternatives for maintaining the uterus in the treatment of atypical invasive placenta. This may be performed by reviewing or examining the prior research that has been done on the subject. The relevance of the challenges that have been highlighted will be demonstrated throughout this paper as its primary objective.

The following requirements were met by researchers in order for them to participate in the study: 1) The paper needs to be written in English and should centre on the topic about chronic kidney disease (CKD) of uncertain etiology in order for it to be considered for publication. 2) The analysed literature includes publications that were published after 2013 but before the time period that this systematic review considers. Editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are virtually similar to already published journal papers are examples of types of research that are not allowed.

Search Strategy

We used "chronic kidney disease" and "uncertain etiology" as keywords.The search for studies to be included in the systematic review was carried out from July, 16th 2023 using the PubMed and SagePub databases by inputting the words: *(("renal insufficiency, chronic"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields] AND "chronic"[All Fields]) OR "chronic renal insufficiency"[All Fields] OR ("chronic"[All Fields] AND "kidney"[All Fields] AND "disease"[All Fields]) OR "chronic kidney disease"[All Fields]) AND ("unknown"[All Fields] OR "unknowns"[All Fields]) AND ("uncertainty"[MeSH Terms] OR "uncertainty"[All Fields] OR "uncertain"[All Fields]) AND ("aetiologie"[All Fields] OR "aetiologies"[All Fields] OR "aetiology"[All Fields] OR "etiologies"[All Fields] OR "etiology"[MeSH Subheading] OR "etiology"[All Fields] OR "causality"[MeSH Terms] OR "causality"[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter]))* used in searching the literature.

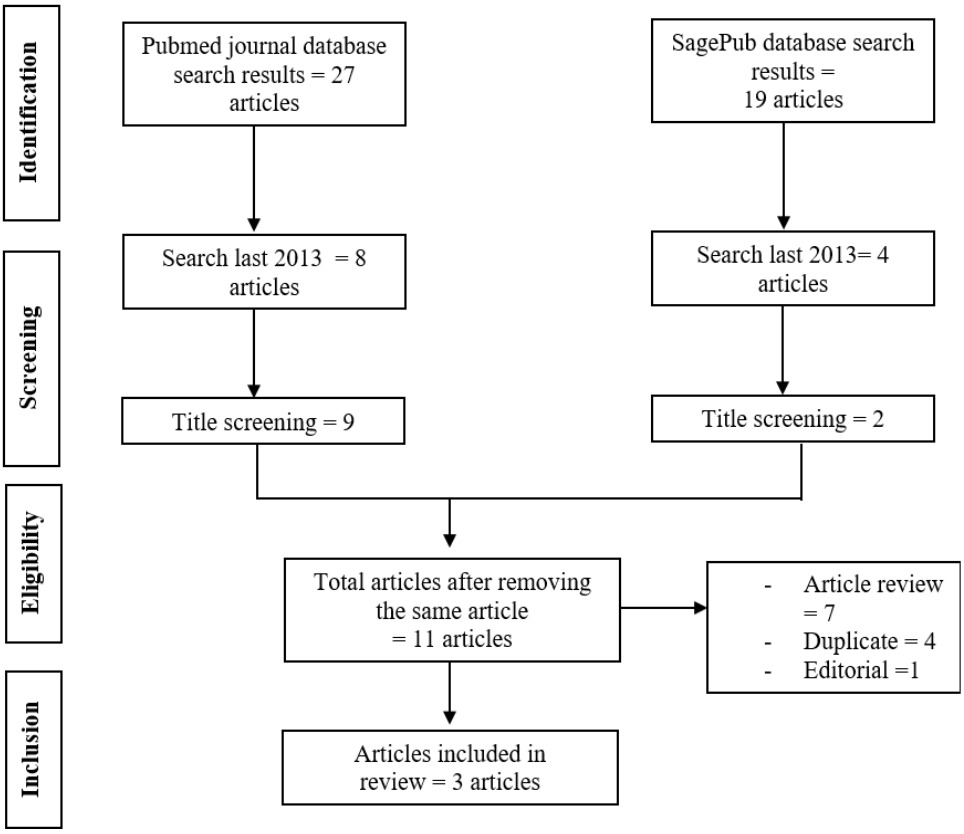

Figure 1. Article search flowchart

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 27 articles, whereas the results of our search on SagePub brought up 19 articles. The results of the search conducted for the last year of 2013 yielded a total 8 articles for PubMed and 4 articles for SagePub. In the end, we compiled a total of 11 papers, 9 of which came from PubMed and 2 of which came from SagePub. We included three research that met the criteria.

Yang, et al (2015)[11] showed leptospira exposure was associated with a decreased eGFR (98.3±0.4 vs 100.8±0.6 ml/min per 1.73 m2, P<0.001) and a greater rate of CKD, particularly at stage 3a-5 (14.4% vs 8.5%) among 3045 survey participants. Leptospiral infection was associated with decreased eGFR in multivariable linear regression (95% CI = -4.15 to -1.93, P < 0.001). In a leptospiral-endemic community, patients with MAT titers >400 had reduced eGFR and higher KIM1/Cr levels (P<0.05). Two participants with chronically elevated MAT titers exhibited urine leptospira DNA and declining renal function.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Yang, 2015[11]	United State of America	Cross-sectional study	3,045 survey participants	Our findings are the first to demonstrate that prolonged human exposure to leptospirosis is strongly linked with the prevalence and severity of chronic kidney disease (CKD), and that this association may lead to a decline in renal function.
Raines, 2014[12]	United State of America	Cross-sectional study	424 respondent	This data reveal a high frequency of chronic kidney disease that is not linked to established risk factors. Instead, they imply that it may be associated with occupational exposure to heat stress in conjunction with inhaling pesticides, chewing sugarcane, and consuming sugar while at work.
Jayatilake, 2013[9]	Sri Langka	Cross-sectional study	877 respondent	These results indicate that individuals in the endemic area are chronically exposed to low levels of cadmium and pesticides via the food chain. Individuals with CKDu have significantly increased urinary cadmium excretion, and the dose–effect relationship between urine cadmium concentration and CKDu stages suggests that cadmium exposure is a risk factor for CKDu pathogenesis. Selenium deficiency and genetic susceptibility observed in patients with CKDu suggest that they may be risk factors for the disease.

Raines, et al (2014)[12] showed prevalence of GFR <60 mL/min/1.73 m2 was 9.8% among women and 41.9% among men (p <0.001). Although systolic and diastolic blood pressure was higher among participants with decreased glomerular filtration rate (p <0.001), hypertension was uncommon. Significant agricultural risk factors for reduced glomerular filtration rate included increased lifetime days cutting sugarcane during the dry season (OR = 5.86, 95% CI = 2.45-14.01), nondeliberate pesticide inhalation (OR = 3.31, 95% CI 1.32-8.31), and sugarcane chewing (OR = 3.24, 95% CI = 1.39-7.58).

Jayatilake, et al (2013)[9] showed the risk of CKD was increased in individuals aged >39 years and those who farmed (chena cultivation) (OR [odds ratio] = 1.926, 95% CI = 1.561 to 2.376 and OR = 1.195, 95% CI = 1.007 to 1.418 respectively, P < 0.05). The risk was reduced in individuals who were male or who engaged in paddy cultivation (OR = 0.745, 95% CI = 0.562 to 0.988 and OR = 0.732, 95% CI = 0.542 to 0.988 respectively, P < 0.05). The mean concentration of cadmium in urine was significantly higher in those with CKDu (1.039 µg/g) compared with controls in the endemic and non-endemic areas (0.646 µg/g, P < 0.001 and 0.345 µg/g, P < 0.05) respectively.

Urine cadmium sensitivity and specificity were 70% and 68.3% respectively (area under the receiver operating characteristic curve = 0.682, 95% CI = 0.61 to 0.75, cut-off value ≥0.397 µg/g). A significant dose–effect relationship was seen between urine cadmium concentration and CKDu stage (P < 0.05). Urine cadmium and arsenic concentrations in individuals with CKDu were at levels known to cause kidney damage. Food items from the endemic area contained cadmium and lead above reference levels. Serum selenium was <90 µg/l in 63% of those with CKDu and pesticides residues were above reference levels in 31.6% of those with CKDu.

DISCUSSION

The lack of a comprehensive classification that encompasses all of the disease's characteristics makes it difficult to explain chronic kidney disease inducing (CKDu). After ruling out all of the potential causes of chronic kidney disease, a patient is given the diagnosis of CKDu in the clinical setting. CKDu can be distinguished from other known causes of CKD based on its shared clinical criteria, which define the condition and set it apart from those causes. The disease is noticed in young and middle-aged individuals, predominantly males, who are involved in physically demanding activities for their means of subsistence, such as agriculture and manual labour.[9]

This disease has been reported in areas across the globe. Proteinuria is either very mild or nonexistent in these people. Patients diagnosed with CKDu are often not diabetic and either have normal blood pressure or simply have modestly elevated blood pressure. The illness is progressive and can develop to chronic kidney disease (CKD) stage 5, which requires treatment with renal replacement therapy over the course of several months. A biopsy of the kidney was conducted on a small number of individuals, and the results showed varied degrees of tubular atrophy and interstitial fibrosis with inflammatory cells.[13]

Table 2. Causes suspected as triggers of CKDu

Cause suspected	References
Chemical coumpound	[9,12]
Pesticide	
Arsenic	
Cadmium	
Physical aspect	[12]
Heat	
Occupations	
Leptospora	[11]

Studies on the aetiology of CKDu have focused on agricultural practises, geographical distribution based on prevalence and incidence, and drinking water pollutants. Environmental, ecological, and health mapping studies have investigated several causes. The distribution and epidemiology suggest the illness is environmental and linked to human activities, particularly agriculture. CKDu may be environmental, but no cause has been found. Geographic spread and study suggest complex aetiology.[5,13] A study showed urine cadmium and arsenic concentrations in individuals with CKDu were at levels known to cause kidney damage.[7,9]

MeN or CKD for an unusual reason is the same as CKD that shows up in farm workers in rural areas, especially those who work on sugarcane farms in Central America. MeN's causes and risk factors are unclear and up for debate, and there isn't a lot of proof available right now. It is thought to be caused by bad living and working situations, such as heat stress, hypovolemia, mineral loss, dehydration, long hours of work without breaks, and wearing clothes, which makes the body heat up. Recently, a strong link has been found between the disease and nickel.[14–16]

Since 1997, Leptospirosis has been recognised as a significant infectious disease in Taiwan, and Leptospira santarosai serovar Shermani is the predominant serovar found. At least 10% of patients with multiple organ dysfunctions in Taiwan are affected by leptospirosis. Acute severe infection may manifest with multiple organ dysfunctions, with fever, jaundice, and acute renal failure constituting the most common triad. Acute renal failure characterised by proximal tubule dysfunction, hypokalemia, and non-oliguria is manifested with primarily acute tubulointerstitial nephritis and acute tubular necrosis on histological examination.[8,11,17]

CONCLUSION

There are several reasons a person can experience CKDu, for example leptosora; physical conditions such as heat and chemical components such as arsenic.

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