

Causes of chronic kidney disease and preventive measure: Rapid evidence reviews

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Abstract

Background: Kidney disease is a silent killer. The prevalence throughout the last 15 years shown a sharp rise. The prevalence of chronic kidney disease in Addis Ababa Public hospital was found to be 38.6%. Thus, this review aimed to summarize the best available evidence on the major factors of CKD.

Methods: A rapid evidence synthesis searched the relevant studies from databases including PubMed, Cochrane, PDQ-Evidence, Health Systems Evidence, and Google scholars. The search engine was built based on the JBI framework for undertaking a mixed-method systematic review (PICO and PICO). Filter applied based on high level of evidence (systematic review, and meta-analysis). The last search was made on September 14, 2024, with no date restriction. Only papers that were published in English language were included in the review. From these databases 287 papers were identified according to the search criteria set. After screening for the titles and abstracts of 46 papers satisfy the inclusion criteria were included in the final review.

Findings: Chronic kidney disease is multi-factorial origin and no certain causes indicated. But the risk factors were contaminated drinking water, a high dietary acid load, contamination of cereals with ochratoxin A and mycotoxins, and temperature, hydration, humidity, attitude, air pollutants, and radiation therapy. In addition, community residing beside petrochemical plants, long-term heavy metal exposure, excessive use of pesticides, low-quality fertilizers, family history, non-alcoholic fatty liver disease, periodontitis, and use of hydroxyethyl starch products. Moreover, lifestyle (smoking, alcohol and obesity), and socio-demographic (men, middle & advanced age, white race, and high-income) were predisposing factors.

The protective factors including reducing salt and low protein intake, increasing fruits and vegetables, anti-oxidants, vitamin D, mega-3 polyunsaturated fats, low-fat dairy and water. Similarly, following DASH dietary guideline, physical exercise professional and technology support, and adherence to medication were controlling factors.

Conclusion: Although there were no direct certain causes, risk factors for CKD were determinant in the water, food, and environment, agricultural activities, illness, drug, genetics, lifestyle, and socio-demographic factors. Protective factors include balanced diet, and clean water. As well, controlling factors includes, physical exercise, professional and technology support, and adherence to proper treatment.

Key words: Chronic Kidney Disease, Water, Food, Soil, Environment

Introduction

Chronic kidney disease (CKD) is defined by either evidence of kidney damage, as indicated by abnormalities in blood or urine markers, or a decreased glomerular filtration rate (GFR) lasting three months or more (KDIGO, 2013). Often described as a "silent killer," CKD may not manifest symptoms until it has significantly progressed (Bailie and Massry, 2005). End-stage renal disease (ESRD), also known as Stage 5 CKD, represents the final stage of kidney failure, requiring dialysis or kidney transplantation for patient survival (CDC 2014).

One subset of CKD is chronic kidney disease of unknown etiology (CKDu), also referred to as

chronic renal failure (CRF). First identified in the 1990s, CKDu has increasingly affected specific geographic regions over the past 15 years (Wanigasuriya et al. 2011). In Ethiopia, the burden of CKD has been notable, with a prevalence of 21.3% reported in Dessie Referral Hospital (Ali et al., 2023), and 38.6% among patients at a public nephrology clinic in Addis Ababa (Kore and Yehuala 2018).

CKD is a growing global health challenge with both known and unknown causes. In high-income countries, it is primarily associated with non-communicable diseases such as hypertension and diabetes (Jha et al. 2013). However, in low- and middle-income regions, additional contributing

factors include infections, environmental toxins, and other unidentified exposures (Stanifer et al., 2014).

This review aims to synthesize current evidence on the risk, protective, and modifiable factors related to CKD. Though CKD has a multifactorial origin and often lacks a single identifiable cause, several potential risk factors, preventive measures, and control strategies have been highlighted in the literature.

Methods

This rapid evidence synthesis was developed in response to a request from the Sidama Regional Health Bureau regarding a potential epidemic in the region. The objective was to provide the best available evidence to inform decision-making by the Ministry of Health, Sidama Regional Health Bureau, and the Sidama Regional State's Bureaus of Water, Mines, and Energy.

A rapid evidence synthesis approach, adapted from the SURE Rapid Response Service, was employed to identify and summarize the best available evidence on factors influencing CKD. A comprehensive search for relevant studies was conducted using the following databases: PubMed, Cochrane Library, PDQ-Evidence, Health Systems Evidence, and Google Scholar. The search strategy was developed based on the Joanna Briggs Institute (JBI) framework for conducting mixed-method systematic reviews, utilizing both the PICO (Population, Intervention, Comparison, Outcome) and PICO (Population, Phenomenon of Interest, Context) models (Aromataris 2024).

Search terms included: (“Kidney Failure” OR “Kidney Disease” OR “Kidney Injury”) AND (“elements in water” OR “Food” OR “Soil” OR “environment”). Studies were selected based on a predefined eligibility criterion that prioritized high-level evidence, including systematic reviews and meta-analyses, regardless of publication year. Only studies published in the English language were included. A total of 287 papers were initially

identified. After title and abstract screening, and the removal of duplicates, 46 studies met the inclusion criteria and were included in the final synthesis.

Inclusion and Exclusion Criteria

This review included only published systematic reviews and meta-analyses that addressed CKD and its associated risk factors or preventive measures. Eligible studies had to be published in the English language, with no restrictions on the year of publication. Studies were considered for inclusion if they reported on potential causal factors, environmental or behavioral exposures, comorbid conditions, or interventions related to CKD prevention, development, or progression.

Studies were excluded if they did not meet the required methodological standards, such as being non-systematic reviews or primary research designs, including cohort studies, case-control studies, cross-sectional studies, case series, and case reports. Additionally, non-research publications such as editorials, letters, commentaries, news articles, communications, reports, and other non-peer-reviewed or non-transparent sources were excluded. Only studies published in English were considered, and any papers in other languages were not included in the final synthesis. The last search for eligible studies was conducted on September 14, 2024.

Findings

The systematic search yielded 287 records from all selected databases. After removing duplicates and screening titles and abstracts, 237 studies were excluded for not meeting the inclusion criteria. The full texts of 50 potentially relevant articles were retrieved and assessed, resulting in the exclusion of 4 studies. Ultimately, 46 systematic reviews and meta-analyses were included in the final synthesis and analysis (Figure 1).

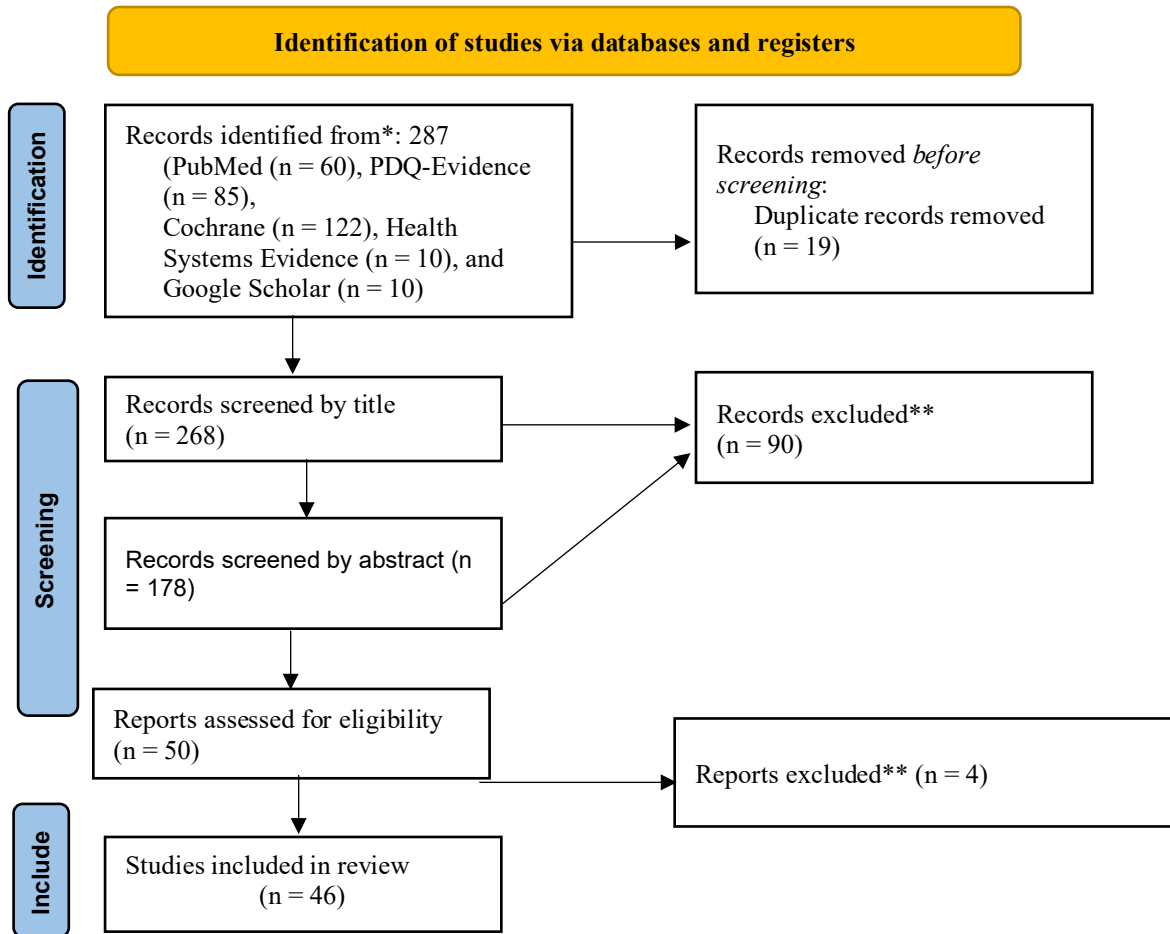


Figure 1: PRISMA flow diagram for the CKD reviews process

Chronic kidney disease is multi-factorial origin and no certain causes indicated. But there was potential predisposing, preventing and controlling factors for CKD.

I. Risk Factors for Chronic Kidney Disease

1. Water-Related Determinants

Limited evidence supports the association between heavy metals in drinking water (e.g., cadmium, lead, chromium) and kidney diseases, with arsenic being a more clearly implicated element (Farkhondeh et al. 2021). Prolonged exposure to fluoride ions and hard water has been linked to kidney injury and fluorosis (Wimalawansa 2014). Additionally, certain algal toxins may cause glomerulo-tubular dysfunction, leading to proteinuria (Wimalawansa 2014). Communities using shallow wells near irrigation systems are particularly at risk (Rajapakse et al., 2016).

2. Food-Related Determinants

Dietary exposures can contribute significantly to CKD. High dietary acid load is associated with both

increased CKD incidence and faster renal decline (Silva et al., 2021). Ochratoxin A and other mycotoxins have also been implicated (Wimalawansa, 2014).

3. Environmental Determinants

Although CKD is increasingly viewed as an environmentally driven condition, no single cause has been definitively identified (Rajapakse et al., 2016). Heat exposure and low altitude are associated with greater CKD risk (Lunyera et al. 2016; Zhang et al. 2024), while extreme temperatures increase the risk of kidney stones and rapid GFR decline (Liu et al., 2021; Rojas-Valverde et al., 2021). Living near petrochemical plants or being exposed to hydrocarbons and air pollutants like PM2.5, PM10, NO₂, and CO correlates with increased CKD risk (Okoye et al. 2022; Ye et al. 2021; Wu et al. 2020; Xu et al. 2024).

Heavy metal exposure—particularly to cadmium, lead, and arsenic—has been associated with CKD progression (Liang et al. 2024). Some inconsistencies exist, particularly regarding lead exposure (Jalili et al. 2021; Moody et al. 2018). Cadmium in blood shows a stronger association with CKD than dietary or urinary levels (Doccioli et al. 2024; Byber et al. 2016). Selenium deficiency has also been noted (Rajapakse et al. 2016).

Radiation therapy for various cancers can result in delayed kidney toxicity (Dawson et al. 2010).

4. Agricultural Practices

While direct evidence linking pesticides to CKD epidemics is sparse, misuse of agrochemicals—particularly low-quality fertilizers and pesticides like glyphosate, AMPA, and chlorpyrifos—has been suggested as a contributing factor (Valcke et al. 2017; Wimalawansa 2014).

5. Genetic Factors

A family history of CKD is a consistent risk factor (Lunyera et al. 2016).

6. Co-morbidities

Non-alcoholic fatty liver disease (NAFLD), periodontitis, and SARS-CoV-2 infection have all been associated with increased CKD risk (Musso et al. 2014; Mantovani et al. 2018; Deschamps-Lenhardt et al. 2019; Silva et al. 2022). Among HIV-positive individuals, low hemoglobin levels significantly contribute to Acute kidney Injury (AKI) (Azagew et al. 2024). Cardiovascular disease and metabolic syndrome (e.g., hypertension, dyslipidemia, insulin resistance) are key contributors (Coca et al. 2012; Overton et al. 2020).

In diabetic patients, factors such as prolonged disease duration, advanced age, uncontrolled blood glucose, and hypertension increase the risk of diabetic nephropathy (Azagew et al. 2024). Hyperuricemia and heavy proteinuria are also linked to CKD progression (Li et al., 2014; Tsai et al., 2016).

7. Medication

Hydroxyethyl starch (HES) increases kidney failure risk by up to 59% (Mutter et al. 2013). Tenofovir disoproxil fumarate also contributes to renal decline (Overton et al. 2020).

8. Lifestyle Factors

Smoking, obesity, excessive alcohol intake, and use of nephrotoxic drugs have all been associated with

CKD progression (Elihimas Junior et al. 2014; Wang et al. 2008; Farkhondeh et al. 2021).

9. Socio-demographic Factors

CKD is more prevalent among men and middle-aged individuals (Lunyera et al. 2016; Tsai et al. 2016). However, obesity-related kidney disease shows a stronger association in women (Wang et al. 2008). Additional risk factors include older age, White ethnicity, and higher-income enrollment regions (Overton et al. 2020).

II. Protective and Controlling Factors

1. Dietary Modifications

Early-stage CKD may benefit from reduced salt intake to control fluid volume (McMahon et al. 2021). Diets rich in fruits, vegetables, antioxidants, vitamin D, and adequate water intake are protective (Wimalawansa 2014). Omega-3-rich seafood and low-fat dairy products are also beneficial (Eslami and Shidfar 2018; Ong et al. 2023). Adherence to the DASH diet has been associated with slower CKD progression (Mozaffari et al. 2020), and very low-protein diets may delay ESRD (Hahn et al. 2020).

2. Physical Activity

Regular exercise improves both physical function and quality of life in CKD patients (Heiwe and Jacobson, 2011).

3. Healthcare and Technology Support

Early diagnosis, prompt referral, and multidisciplinary care are crucial in slowing CKD progression (Kirsztajn et al. 2011). Pharmacist-led interventions and home blood pressure monitoring have been shown to enhance disease control (Nakanishi et al. 2021; Muneer et al. 2022). Nutritional mobile apps are also effective tools in self-management (Kosa et al. 2019; Campbell and Porter 2015).

4. Pharmacological Interventions

Dulaglutide has shown promise in improving renal outcomes in CKD patients with diabetes (Tuttle et al., 2021). Finerenone significantly reduced CKD progression in patients with type 2 diabetes (Rossing et al., 2022). Prostaglandin E1 (PGE1) may reduce proteinuria in diabetic kidney disease (Wang et al., 2010).

Ethics approval and consent to participate: Since this review involved collecting, reviewing and summarizing publicly available data, this study did not require ethics approval from an Institutional Review Board (IRB).

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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References

- Ali A, Mulatu K, Feleke SF & Wassie GT (2023). *Prevalence of chronic kidney disease and associated factors among patients with underlying chronic disease at Dessie Referral Hospital, East Amhara Region, Ethiopia*. *Frontiers in Epidemiology*, 3, p.1154522.
- Aromataris E, Lockwood C, Porritt K, Pilla B & Jordan Z (2024). *JBIManual for Evidence Synthesis*. Adelaide: JBI.
- Azagew AW, Abate HK, Ferede YM & Mekonnen CK (2024). *Acute kidney injury and its predictors among HIV-positive patients in Africa: Systematic review and meta-analysis*. *PLoS ONE*, 19(2). p.e0298302.
- Azagew AW, Beko ZW & Mekonnen CK (2024). *Determinants of diabetic nephropathy among diabetic patients in Ethiopia: Systematic review and meta-analysis*. *PLoS ONE*, 19(2). p.e0297082.
- Bailie GR & Massry SG (2005). Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease: An Overview. *Kidney International Supplements*, 67(1). pp. S1–S120.
- Byber K, Lison D, Verougstraete V, Dressel H & Hotz P (2016). Cadmium or cadmium compounds and chronic kidney disease in workers and the general population: A systematic review. *Critical Reviews in Toxicology*, 46(3): 191–240.
- Campbell J & Porter J (2015). Dietary mobile apps and their effect on nutritional indicators in chronic renal disease: A systematic review. *Nephrology (Carlton)*, 20(10): 744–751.
- CDC (Centers for Disease Control and Prevention) (2014). National Chronic Kidney Disease Fact Sheet: General Information and National Estimates on Chronic Kidney Disease in the United States. Atlanta: U.S. Department of Health and Human Services.
- Cheru Kore H & Yehuala Y (2018). Prevalence of chronic kidney disease and associated factors among patients with kidney problems in public hospitals in Addis Ababa, Ethiopia. *Journal of Kidney*, 4(1).
- Coca SG, Singanamala S & Parikh CR (2012). Chronic kidney disease after acute kidney injury: A systematic review and meta-analysis. *Kidney International*, 81(5), pp.442–448.
- Dawson LA, Kavanagh BD, Paulino AC, Das SK, Miften M, Li XA, et al. (2010). Radiation-associated kidney injury. *International Journal of Radiation Oncology, Biology, Physics*, 76(3 Suppl). pp. S108–S115.
- Deschamps-Lenhardt S, Martin-Cabezas R, Hannedouche T & Huck O (2019). Association between periodontitis and chronic kidney disease: Systematic review and meta-analysis. *Oral Diseases*, 25(2): 385–402.
- Doccioli C, Liang KH, Feng J, Wu C, Wei J, Lv J, Dong Y & Chen Z (2024). Association of cadmium environmental exposure with chronic kidney disease: A systematic review and meta-analysis. *Science of the Total Environment*, 906, p.167165.
- Elihimas Junior UF, Elihimas HCS, Lemos VM, Leão MA, Sá MPBO, França EET, Lemos A, Valente LM & Markman Filho B (2014). Smoking as risk factor for chronic kidney disease: Systematic review. *Jornal Brasileiro de Nefrologia*, 36(4): 519–528.
- Eslami O & Shidfar F (2018). Dairy products and chronic kidney disease: Protective or harmful? A systematic review of prospective cohort studies. *Nutrition*, 55–56: 21–28.
- Farkhondeh T, Naseri K, Esform A, Aramjoo H & Naghizadeh A (2021). Drinking water heavy metal toxicity and chronic kidney diseases: A systematic review. *Reviews on Environmental Health*, 36(3): 359–366.
- Hahn D, Hodson EM & Fouque D (2020). Low protein diets for non-diabetic adults with chronic kidney disease. *Cochrane Database of Systematic Reviews*, (10).
- Heiwe S & Jacobson SH (2011). Exercise training for adults with chronic kidney disease. *Cochrane Database of Systematic Reviews*, (10).
- Jalili C, Azimi H, Haghani H, Rashtchizadeh N, Nasri P, Pourafkari L & Jalilian M (2021). Associations between exposure to heavy metals and the risk of chronic kidney disease: A systematic review and meta-analysis. *Critical Reviews in Toxicology*, 51(2): 165–182.

- Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY & Yang CW (2013). Chronic kidney disease: Global dimension and perspectives. *The Lancet*, 382(9888): 260–272.
- KDIGO (kidney disease: Improving Global Outcomes) (2013). KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney International Supplements*, 3(1): 1–150.
- Kirsztajn GM, Pecoits-Filho R, Cuppari L, Heilberg IP, Draibe SA, Bregman R, Monteiro PA, Sesso R & Canziani MEF (2011). Chronic kidney disease: Importance of early diagnosis, immediate referral and structured interdisciplinary approach to improve outcomes in patients not yet on dialysis. *Jornal Brasileiro de Nefrologia*, 33(1): 93–108.
- Kosa SD, Sikka M, Bajpai RK, Tripathi KK, Joshi HK & Singh AK (2019). Nutritional mobile applications for CKD patients: Systematic review. *Kidney International Reports*, 4(3): 399–407.
- Li L, Chu Y, Zhao Y, Zeng X, Liu F & Fu P (2014). Is hyperuricemia an independent risk factor for new-onset chronic kidney disease? *BMC Nephrology*, 15(122): 1–12.
- Liang KH, Doccioli C, Feng J, Wu C, Wei J, Lv J, Dong Y & Chen Z (2024). The general external exposome and the development or progression of chronic kidney disease: A systematic review and meta-analysis. *Environmental Pollution*, 358, p.124509.
- Liu J, Zhu G, Shen J, Liu X, Ding Y, Chen J, Chen C & Liu Y (2021). Hot weather as a risk factor for kidney disease outcomes: A systematic review and meta-analysis. *Science of the Total Environment*, 801, p.149806.
- Lunyer J, Stanifer JW, McClellan W, Anand S & Patel UD (2016). CKD of uncertain etiology: A systematic review. *Clinical Journal of the American Society of Nephrology*, 11(3): 379–385.
- Mantovani A, Csermely A, Andriulli A, Dalla V, Malavazos AE, Dossena M, Colombo L, Perna S, Spinass GA & Monardo P (2018). Nonalcoholic fatty liver disease increases risk of incident chronic kidney disease: A systematic review and meta-analysis. *Metabolism*, 79: 64–76.
- McMahon EJ, Campbell KL, Bauer JD, Krishnan M & Chauveau P (2021). Altered dietary salt intake for people with chronic kidney disease. *Cochrane Database of Systematic Reviews*, (6).
- Moody EC, Coca SG & Sanders AP (2018). Toxic metals and chronic kidney disease: A systematic review of recent literature. *Current Environmental Health Reports*, 5(4): 453–463.
- Mozaffari H, Ajabshir S & Alizadeh S (2020). Dietary approaches to stop hypertension and risk of chronic kidney disease: A systematic review and meta-analysis of observational studies. *Clinical Nutrition*, 39(7): 2035–2044.
- Muneer S, Aboud S, Chaudhary K, Bhat H, Rizwan M, Hussain M, Khalid M, Ahmad R & Abid M (2022). Impact of home telemonitoring and management support on blood pressure control in no dialysis CKD: A systematic review and meta-analysis. *Canadian Journal of Kidney Health and Disease*, 9, p.20543581221106248.
- Mutter TC, Ruth CA & Dart AB (2013). Hydroxyethyl starch (HES) versus other fluid therapies: Effects on kidney function. *Cochrane Database of Systematic Reviews*, (7).
- Nakanishi M, Kato K, Ando K, Watanabe H, Hirata T, Fujimura A, et al., (2021). Impact of pharmacist intervention for blood pressure control in patients with chronic kidney disease: A meta-analysis of randomized clinical trials. *Journal of Clinical Pharmacy and Therapeutics*, 46(1): 114–120.
- Okoye OC, Carnegie E & Mora L (2022). Air pollution and chronic kidney disease risk in oil and gas-situated communities: A systematic review and meta-analysis. *International Journal of Public Health*, 67, p.1604522.
- Ong KL, Yusuf S, Perkovic V, Arnett DK, Barzilay JI, Chang TI, et al. (2023). Association of omega-3 polyunsaturated fatty acids with incident chronic kidney disease: Pooled analysis of 19 cohorts. *BMJ*, 380, p.e072909.
- Overton ET, DeJesus E, Tebas P, McComsey GA, Sax PE, Tierney C, (2020). An evaluation of baseline kidney function in the REPRIEVE trial of pitavastatin in human immunodeficiency virus. *Journal of Infectious Diseases*, 222(Suppl 1): S41–S51.
- Rajapakse S, Shivanthan MC & Selvarajah M (2016). Chronic kidney disease of unknown etiology in Sri Lanka. *International Journal of Occupational and Environmental Health*, 22(3): 259–264.
- Rojas-Valverde D, et al. (2021). Exertional rhabdomyolysis and acute kidney injury in endurance sports: A systematic review. *European Journal of Sport Science*, 21(2): 261–274.