

## HYPERTENSION AND CHRONIC KIDNEY DISEASE : A SYSTEMATIC REVIEW

**Kgs. Mahendra Effendy\***

*\*University of Lampung, Indonesia, kgsmahendraeffendy@gmail.com*

**\*Corresponding Author:**

*kgsmahendraeffendy@gmail.com*

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### **Abstract**

*The frequency of chronic kidney disease, often known as CKD, is on the rise and affects 10–15% of the population around the world. Approximately one percent of adult Americans are affected by chronic kidney disease (CKD). The presence of reduced kidney function (an estimated glomerular filtration rate [eGFR] of less than 60 mL/min/1.73 m<sup>2</sup>) or kidney damage (usually demonstrated by the presence of proteinuria) that has lasted for more than three months is what is considered to be chronic kidney disease (CKD). At the moment, hypertension, a problem that has an effect on public health on a global scale, is the leading contributor to the overall illness burden. It is the single most significant modifiable risk factor that contributes to cardiovascular disease, stroke, and renal failure. Uncontrolled hypertension is linked to a higher risk of developing chronic kidney disease (CKD), which is also regarded to be a consequence of hypertension that is not under control. One of the most common factors leading to CKD is hypertension. The connection between high blood pressure and chronic renal disease is a convoluted one that elevates the probability of negative outcomes in the cardiovascular and cerebrovascular systems. According to the findings of this study, the percentage of hypertension patients who also have CKD is significantly higher than that of patients in the other groups. Additionally, the mean systolic and diastolic blood pressure of patients with CKD was found to be higher than that of those who did not have CKD.*

**Keyword:** *Blood Preassure; Chronic Kidney Disease; Hypertension*

**INTRODUCTION**

Chronic Kidney Disease (CKD) is a structural or functional disorder of the kidney that has been present for at least three months, is progressive and irreversible, and is accompanied by multiple metabolic disorders.<sup>1</sup> Chronic Kidney Disease, also known as CKD, is an umbrella term that refers to a decline in kidney function of any severity, ranging from mild to moderate to severe chronic kidney damage.<sup>2</sup> One in ten American adults, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), has CKD at any stage.<sup>3</sup>

Chronic kidney disease (CKD) affects 10–15% of the population worldwide, and its prevalence is increasing. In the United States, CKD affects around 1% of adults. CKD is defined as the presence of impaired kidney function (an estimated glomerular filtration rate [eGFR] of less than 60 mL/min/1.73 m<sup>2</sup>) or kidney damage (typically evidenced by the presence of proteinuria) that has persisted for more than three months.<sup>4–6</sup> A blood pressure (BP) of 140/80 mmHg is considered to be hypertension by the European Society of Cardiology and the European Society of Hypertension (ESC/ESH).<sup>2</sup>

This condition affects approximately thirty percent of the general adult population and as many as ninety percent of those who have CKD. In addition to being a cause and an effect of chronic kidney disease (CKD), hypertension also plays a role in the course of the disease.<sup>7,8</sup> The incidence and severity of hypertension both rise in tandem with a declining eGFR. In addition, both high blood pressure and chronic kidney disease are independent risk factors for cardiovascular illness (CVD). When both are present at the same time, the risks of morbidity and mortality from cardiovascular disease are significantly elevated.<sup>8–11</sup>

Those who have stage 3 (eGFR 30–59 mL/min/1.73 m<sup>2</sup>) or stage 4 (eGFR 15–29 mL/min/1.73 m<sup>2</sup>) chronic kidney disease (CKD), as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, have a higher risk of dying from cardiovascular disease (CVD) than they do of progressing to end-stage renal disease (ESRD) (eGFR). Importantly, from a therapeutic standpoint, reducing blood pressure can halt the decline of estimated glomerular filtration rate (eGFR), delay development to end-stage renal disease (ESRD), and minimize the incidence of cardiovascular disease (CVD) in this patient population.<sup>8,10,11</sup>

This article investigate the connection between hypertension and CKD, we choose to carry out this research.

**METHODS**

**Protocol**

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 checklist served as the basis for developing the principles that guided the conduct of this systematic review.

**Eligibility Criteria**

This systematic review was written with the purpose of analyzing studies on the topics of "Hypertension" and "Chronic Kidney Injury". These are the topics that were discussed in the studies that were analyzed. The following are the criteria that must be met in order to have your writing included: 1) Articles have to be available online in their entirety; 2) Articles have to be written in English; and 3) Articles have to have been published after the year 2012 and up until the point in time when this systematic review is written. The following kinds of textual submissions will not be accepted under any circumstances: 1) Editorial letters; 2) submissions that do not contain a Digital Object Identifier (DOI); and 3) Article reviews and submissions that are comparable to these types of submissions.

**Search Strategy**

The search for studies to be included in the systematic review was carried out from November 10-16<sup>th</sup>, 2022 using the PubMed, SagePub, and Clinical Key databases by inputting the words: "Hypertension" and "Chronic Kidney Injury". Where ("hypertense"[All Fields] OR "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR "hypertension s"[All Fields] OR "hypertensions"[All Fields] OR "hypertensive"[All Fields] OR "hypertensive s"[All Fields] OR "hypertensives"[All Fields]) AND ("chronic"[All Fields] OR "chronical"[All Fields] OR "chronically"[All Fields] OR "chronicities"[All Fields] OR "chronicity"[All Fields] OR "chronicization"[All Fields] OR "chronics"[All Fields]) AND ("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields] OR "kidney s"[All Fields]) AND ("injurie"[All Fields] OR "injured"[All Fields] OR "injuries"[MeSH Subheading] OR "injuries"[All Fields] OR "wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "injurious"[All Fields] OR "injury s"[All Fields] OR "injured"[All Fields] OR "injurys"[All Fields] OR "injury"[All Fields]) is used as search keywords.

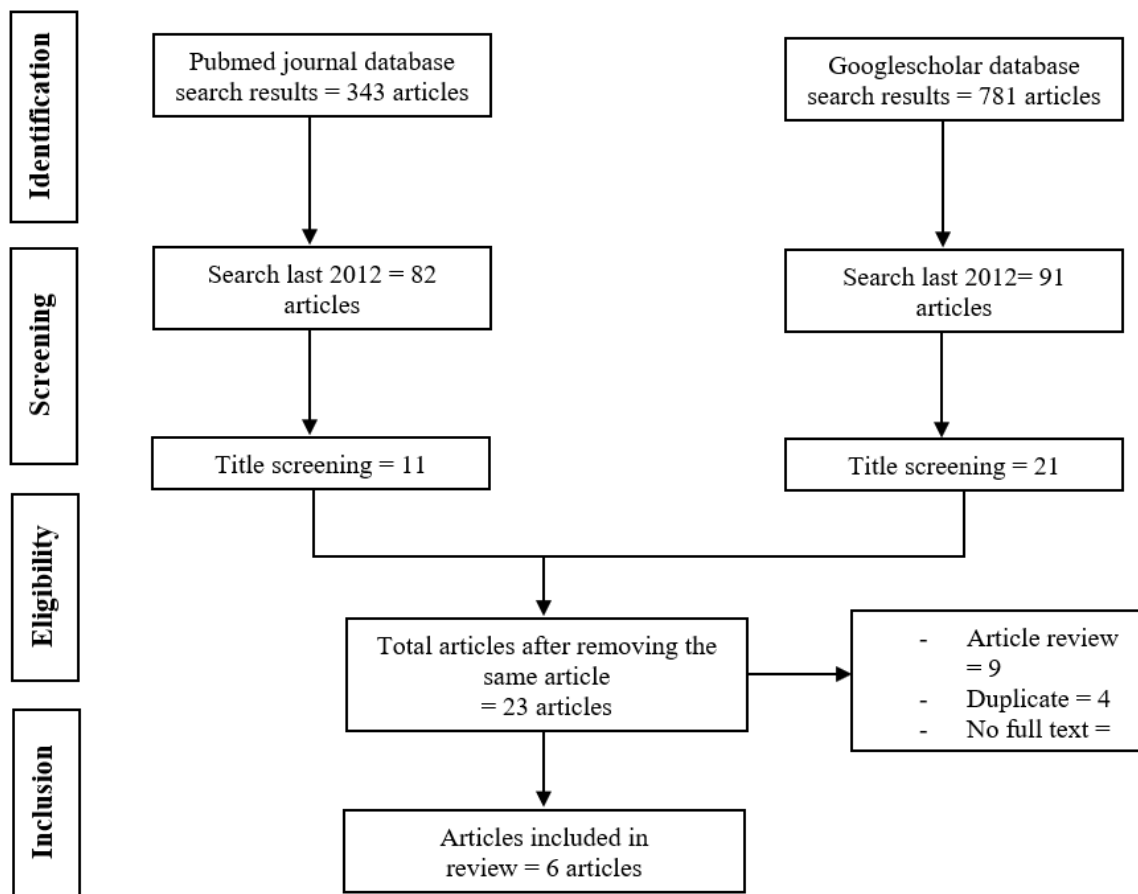


Figure 1. Article search flowchart

**Data retrieval**

Following the completion of a literature search, in which the titles and abstracts of previously published studies were read, the author revised the criteria for what should be included and what should be excluded from the study. Only the studies that were able to meet all of the requirements were taken into consideration for inclusion in the systematic review. It is possible to collect information in the form of a title, author, publication date, origin of study location, research study design, and research variables in each individual study. This information is laid out in a particular format for your perusal.

**Quality Assessment and Data Synthesis**

To determine which studies might be eligible for consideration, the authors conducted their own independent reviews of a selection of the studies found in the articles' titles and abstracts. Following this, the full texts of the studies that qualify for inclusion in the systematic review will be read in order to determine which studies can be used as final inclusions for the purpose of the review.

**RESULT**

The participants were divided into the following four stages of hypertension: normotension (n = 586, 27.3%), pre-hypertension (n = 815, 37.9%), stage 1 hypertension (n = 386, 18.0%), and stage 2 hypertension (n = 363, 16.9%). There were 461 cases of chronic kidney disease that were identified throughout the course of a follow-up period that averaged 6.5 years (14,023 person-years). Adjusted hazard ratios of chronic kidney disease were considerably greater for individuals with pre-hypertension (1.49, P 0.003), stage 1 (1.83, P 0.001), and stage 2 (2.55, P 0.001) hypertension when compared to normotension. It was determined that the population-attributable proportion of pre-hypertension (12.1%) was comparable to that of hypertension stages 1 (8.6%) and 2 (14.9%).<sup>12</sup>

Among male subjects, adjusted predictors of developing CKD included aging, hypertension, high normal BP (which had significantly higher risk than in women), eGFR, new diagnosed diabetes [2.48(1.37–4.51)]; interestingly abdominal obesity decreased the risk of CKDs3-5 about 30% which was marginally significant. Finally, in the whole population, in which the female gender per se was associated with more than tripling risk of CKD compared with men (3.17, 95% CI 2.44–4.12), age, eGFR, known diabetes, current smoking and hypertension were independent predictors.<sup>13</sup>

The hazard ratios (95% confidential intervals) for chronic kidney disease in the prehypertension group were 1.25 (1.02–1.85), in the undiagnosed hypertension group they were 1.62 (1.07–2.79), and in the diagnosed hypertension group they were 1.98 (1.15–3.96) When compared to the normotension group, the prehypertension group had a 1.25 (1.02–1.85), the undiagnosed hypertension group had a 1.62.<sup>14</sup>

The cumulative incidence of chronic kidney disease was significantly different across the various blood pressure categories, as demonstrated by the Kaplan–Meier curves (log-rank test,  $P < 0.001$  for each). According to the Cox proportional hazard analysis, the independent risk variables for chronic kidney disease were a person's age, their estimated glomerular filtration rate (eGFR), their systolic blood pressure, and their diastolic blood pressure. It was discovered that 2.4% of the participants with CKD occurrences had an elevated incidence that could be attributed to prehypertension.<sup>14</sup> Yano *et al* study's with three-year follow-up period showed the incidence rates of hypertension among participants with optimal BP (<120/80 mmHg,  $n = 18,724$ ), normal BP (120–129/80–84 mmHg,  $n = 15,017$ ) and high-normal BP (130–139/85–89 mmHg,  $n = 11,637$ ) were 8, 23, and 39% in men, and 6, 20, and 37% in women, respectively.. Participants who had new-onset hypertension had a higher risk for proteinuria [odds ratio (95% confidence interval) 1.7 (1.3–2.3) in men and 1.6 (1.2–2.2) in women], but not for eGFR below 60 ml/min per 1.73 m<sup>2</sup> when compared with those who maintained optimal BP during follow-up. This was the case regardless of the classifications of their blood pressure at the beginning of the study. During the follow-up period, men whose blood pressure stayed within the high-normal range had an increased likelihood of developing proteinuria [odds ratio (95% confidence interval) = 1.6 (1.1–2.3)], but not an eGFR that was lower than 60 ml/min per 1.73 m<sup>2</sup>.<sup>15</sup>

**Table 1.** The litelature include in this study

Author	Origin	Method	Period	Sample Size / Characteristic	Result
Kanno, 2012 <sup>12</sup>	Japan	Cohort prospective	2002-2010	2150 people who do not already have CKD	461 cases of CKD were documented during 6.5 years (14,023 person-years). Pre-hypertension (1.49, $P < 0.003$ ), Stage 1 (1.83, $P < 0.001$ ), and Stage 2 (2.55, $P < 0.001$ ) hypertension had greater adjusted CKD hazard ratios than normotension. Pre-hypertension (12.1%) is comparable to Stage 1 (8.6%) and Stage 2 (14.9%) hypertension.
Tohidi, 2012 <sup>13</sup>	Iran	Cohort retrospective	1999-2001	6,437 patient	Among male subjects, adjusted predictors of developing CKD included aging, hypertension, high normal BP (which had significantly higher risk than in women), eGFR, and newly diagnosed diabetes [2.48(1.37–4.51)]; interestingly, abdominal obesity decreased the risk of CKDs3-5 about 30%, which was marginally significant. Finally, in the whole population, in which the female gender per se was associated with more than tripling risk of CKD compared with men (3.17, 95% CI 2.44–4.12), age, eGFR, known diabetes,current smoking and hypertension were independent predictors.
Cao, 2014 <sup>14</sup>	China	Cohort prospective	2006-2011	1,703 white-collar workers without preexisting CKD	Compared with normotension, the hazard ratios for CKD in prehypertension, undiagnosed hypertension, and diagnosed hypertension were 1.25 (1.02–1.85), 1.62 (1.07–2.79), and 1.98 (1.15–3.96). The cumulative incidence of CKD differed significantly between blood pressure categories (log-rank test, $P < 0.001$ ). Age, eGFR, systolic and diastolic blood pressure were independent CKD risk variables, according to Cox proportional hazard analysis. 2.4% of CKD individuals had high prehypertension incidence.
Yano, 2014 <sup>15</sup>	Japan	Cohort prospective	2008-2011	45,378 patients	Irrespective of the baseline BP classifications, participants with new-onset hypertension had a higher risk for proteinuria [odds ratio (95% confidence interval) 1.7 (1.3–2.3) in men and 1.6 (1.2–2.2) in women], but not for eGFR below 60 ml/min per 1.73 m <sup>2</sup> , compared with those who maintained optimal BP during follow-up. Men who remained in the high-normal BP range during follow-up showed higher risk for proteinuria [odds ratio (95% confidence interval) 1.6 (1.1–2.3)], but not for eGFR below 60 ml/min per 1.73 m <sup>2</sup> .
Xue, 2015 <sup>16</sup>	China	Cohort prospective	July 2006 to October 2007	20,034 with prehypertension and 12,351 with ideal blood pressure	Multivariate Cox Regression showed that relative risks (RRs) for new onset CKD were 1.69 (95% CI: 1.412-0.4, $P = 0.001$ ) greater in the prehypertensive cohort than in the ideal blood pressure population. Adjusted for established CV risk variables, the risks were 1.68 (95% CI: 1.332.13 $P = 0.001$ ) times higher in females and 2.14 times higher in males.
Wan, 2019 <sup>17</sup>	Hong Kong	Population-based retrospective cohort study	October 1, 2011, and March 31, 2012	267,469 adult patients with hypertension	A 10 mm Hg increase in repeated systolic blood pressure was linked to an increased risk of cardiovascular disease and chronic renal disease by 16% (hazard ratio, 1.15; 95% confidence interval, 1.13-1.16), 11% (1.11; [1.08-1.13]), and 22% (1.22; [1.20-1.24]), respectively.

The Kaplan-Meier in Xue<sup>16</sup> study was utilized in order to conduct an analysis of cumulative survival as well as independence from the incidence of new CKD events. The influence of prehypertension on chronic kidney disease was investigated with the use of multivariate Cox regression. The median amount of time spent following up was 47 months, with the interquartile range ranging from 44 to 51 months. During the time of follow-up, there were a total of 601 cases with CKD that were newly diagnosed. The prehypertensive cohort had a cumulative incidence of new CKD events that

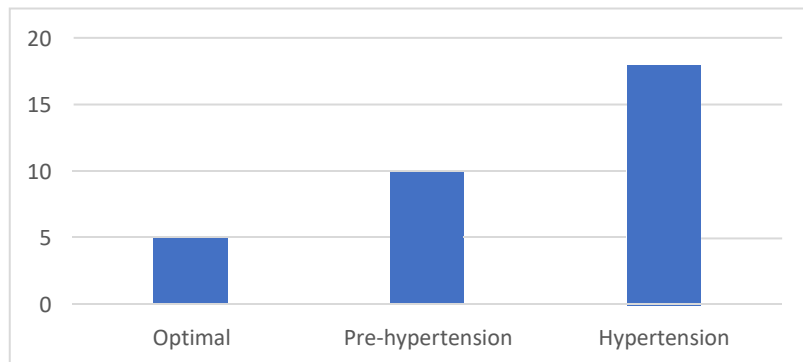
was 2.10% greater than that of the population with optimum blood pressure ( $P = 0.0001$ ); this difference was statistically significant.

The results of a multivariate Cox regression showed that the relative risks (RRs) for the new onset of CKD events in the population of prehypertensive individuals were 1.69 (95% CI: 1.412-0.04,  $P = 0.001$ ) times higher than those in the population of individuals with ideal blood pressure. When adjusted for traditional cardiovascular risk factors, the risks were 1.68 times higher in females (95% CI: 1.33–2.13;  $P = 0.001$ ) and 2.14 times higher in males (95% CI: 1.58–2.91;  $P = 0.001$ ) respectively. Prehypertension was shown to be an independent risk factor for the development of new cases of CKD in the Chinese population, as the researchers' findings showed.<sup>16</sup> Wan *et al* study showed repeated increases of 10 mm Hg in systolic blood pressure were associated with an increased risk of cardiovascular disease and chronic kidney disease of 16% (hazard ratio, 1.15; [95% CI, 1.13–1.16]), 11% (1.11; [1.08–1.13]), and 22% (1.22; [1.20–1.24]), respectively. This was the case for the composite of cardiovascular disease and chronic kidney disease.<sup>17</sup>

**DISCUSSION**

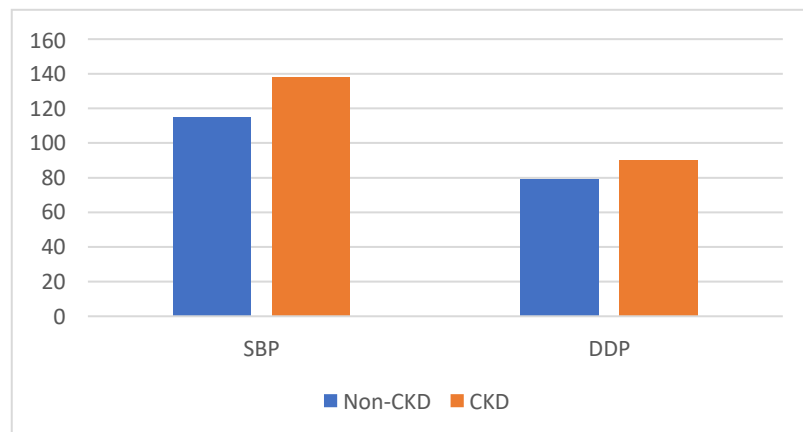
At this time, hypertension, an issue that affects public health on a global scale, is the primary contributor to the overall burden of disease. It is the most important risk factor that can be changed that contributes to cardiovascular disease, stroke, and renal failure. Both uncontrolled hypertension and chronic kidney disease (CKD) are considered to be complications of uncontrolled hypertension. Hypertension is a prominent cause of CKD. The connection between hypertension and chronic kidney disease is a complicated one that raises the likelihood of unfavorable outcomes in the cardiovascular and cerebrovascular systems.<sup>18</sup>

After multiple checks, a person is considered to have hypertension if their systolic blood pressure (also known as TDS) is greater than 140 mm Hg and/or their diastolic blood pressure (also known as TDD) is greater than 90 mm Hg. Everyone over the age of 18 is considered an adult according to this definition.<sup>19</sup> Chronic kidney disease (CKD) has a detrimental effect on long-term health outcomes since it raises the risk of cardiovascular diseases and accelerates the progression of renal failure. As a consequence of this, CKD is widely acknowledged as a significant health issue, and despite advancements in renal-based therapy for the treatment of conditions such as high blood pressure, glomerulonephritis, and diabetes, the global burden of CKD as well as the number of people who are diagnosed with it are both rising.<sup>20</sup>



**Figure 2.** Percentage of normotensive, prehypertensive, and hypertensive patients to the occurrence of CKD

It is currently unknown how prehypertension contributes to the development of CKD. An earlier study found that prehypertension had a substantial association with renal arteriosclerosis when measured by kidney biopsy. This finding suggests that renal arteriosclerosis may be a potential pathophysiologic cause. In addition, it was discovered that high blood pressure contributed to the progression of renal arteriosclerosis, glomerular sclerosis, and renal arteriolar hyalinosis. These conditions, which may lead to decreased renal perfusion and renal ischemia, ultimately contribute to a reduction in renal function. These findings may help to explain, at least in part, how prehypertension contributes to chronic kidney disease.<sup>21,22</sup>



**Figure 3.** Comparison of blood pressure in CKD and non-CKD patients

CKD is linked to both overt and covert forms of vascular disease, as well as to the progression of atherosclerosis and the natural age-related loss in renal function (which may be a consequence of atherosclerosis). Pre-hypertension was found to be independently linked with renal arteriosclerosis and arteriolar hyalinosis after morphological examination was performed as a consequence of a renal biopsy.<sup>23,24</sup> Even after accounting for traditional cardiovascular risk variables in Japanese population-based autopsy samples, such as total cholesterol, glucose intolerance, BMI, habitual smoking, and alcohol intake, the link remained.<sup>12,22</sup>

This was the case even after taking into account the findings. In a study that was very similar to the one that was done for IgA nephropathy and was based on a renal biopsy, pre-hypertension was found to have a strong relationship to the severity of mesangial proliferation as well as arteriolar sclerosis, which included intimal thickening and hyalinosis. A sustained increase in systemic blood pressure can generate pathological alterations such as atherosclerosis, which can cause a disruption in renal perfusion and renal ischemia, ultimately leading to a deterioration in renal function.<sup>25,26</sup>

## CONCLUSION

This study shows that the percentage of hypertensive patients with CKD is higher than the other groups. In addition, the mean systolic and diastolic blood pressure of CKD patients was higher than non-CKD patients.

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