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METABOLIC SYNDROME AND PROGESSION OF CHRONICKIDNEY DISEASE : A SYSTEMATIC REVIEW

Stephanie Talilah*

**Faculty of Medicine, Indonesian Christian University*

Corresponding Author:-
stephytalilah@yahoo.co.id

Abstract

Indicators of metabolic function, cardiovascular health, and inflammation are all components of the metabolic syndrome, which is a cluster of risk factors. The metabolic syndrome is defined and characterized in a variety of different ways, depending on who you ask. Individuals are considered to have metabolic syndrome (MetS) when multiple risk factors for chronic kidney disease, such as obesity, hyperglycemia, hypertension, and dyslipidemia (high triglyceride and low HDL-C), co-occur within the same person. These risk factors include high triglyceride levels and low HDL-C levels. A high level of triglycerides and a low level of HDL-C are two of these risk factors. A mechanistic explanation for MetS as a cause of CKD would be more convincing than simply stating that the two conditions are connected. Research is absolutely necessary if "black boxes" are to be removed from any postulated chain of causality connecting metabolic syndromeand chronic kidney disease. It has been demonstrated that metabolic syndrome is a risk factor for a number of chronic diseases that are not contagious, some of which are diabetestype 2, coronary heart disease, stroke, and chronic kidney disease. According to the information that we have, hypertension is the factor that contributes to metabolic syndrome more frequently than any other, which leads to CKD.

Keyword: *Chronic Kidney Disease; Diabetes; Hypertension; Lipid; Metabolic Syndrome*

INTRODUCTION

Metabolic syndrome is a group of risk factors that includes metabolic, vascular,and inflammatory indicators. There are several definitions used to describe and characterize the metabolic syndrome.[1] The metabolic disorders that underlie consistent metabolic syndrome, such as atherogenic dyslipidemia, increased blood pressure (BP), insulin resistance, obesity, and pro-thrombotic and pro-inflammatory states. While someexpert definitions consider obesity as an important criterion, other definitions focus mostly on insulin resistance.[2]

Metabolic syndrome (MetS) is a condition in which a person has high blood pressure, central obesity and dyslipidemia, with or without hyperglycemia. If these conditions are present in one person at the same time, then that person has a high risk ofmacrovascular disease.[3] Obesity occurs due to an imbalance between energy intake and energy expenditure, resulting in excess energy which is then stored in the form of fat tissue.[4] Various organizations have provided different definitions, but all study groups agree that obesity, insulin resistance, dyslipidemia and hypertension are major components of MetS.[3]

Chronic kidney disease, also known as CKD, is an issue that affects public health all over the world.[5,6] Metabolic syndrome (MetS) is a pathological state in which multiple risk factors for chronic kidney disease, such as obesity, hyperglycemia, hypertension, and dyslipidemia (high triglyceride and low HDL-C), co-occur within individuals. These risk factors include high triglyceride levels and low HDL-C. Metabolic syndrome has been demonstrated to be a risk factor for a number of chronic diseases that are not contagious,including diabetes type 2, coronary heart disease, stroke, and chronic kidney disease (CKD).[7,8]

In the past ten years, numerous research have been conducted to investigate the link between MetS and CKD. The incidence rate of MetS is on the rise, and over the pastfew years, the prevalence of chronic kidney disease (CKD) has shown a steady annual increase. Both of these trends pose a significant risk to human life and health, as well as an economic burden on society and families, and they lower the quality of life of those who are afflicted with the conditions. Clinicians need to be on the lookout for multiple sclerosis and chronic kidney disease in patients who are middle-aged and elderly becausethese age groups are more likely to suffer from chronic non-communicable diseases.[9,10]

This study presented evidence that supports the hypothesis that metabolic syndrome is linked to chronic renal disease.

METHODS

Protocol

We followed to the Preferred Reporting Items for Systematic Review and Meta- Analysis (PRISMA) 2020 checklist throughout the entire process of conducting this systematic review. On top of these guiding principles, which served as the foundation, the rules governing the procedure for conducting this systematic review were developed. These rules served as the basis.

Eligibility Criteria

This systematic review was developed to analyze papers on "metabolic syndrome"and "chronic kidney disease". These are the topics that were extensively covered in the study that was considered. In order for your work to be considered, the following conditions must be met: 1) Articles must be written in the English language. 2) Articles must have been published after 2012, but prior to the creation of this systematic review. Under no circumstances will the following types of textual contributions be considered for inclusion in the anthology: 1) Editorial letters, 2) submissions without a Digital Object Identifier (DOI), and 3) article reviews and submissions similar to those previously published in the journal.

Search Strategy

The search for studies to be included in the systematic review was carried out from December, 1st 2022 using the PubMed and SagePub databases by inputting the words "metabolic syndrome" and "chronic kidney disease". Where ((("metabolic syndrome"[MeSH Terms] OR ("metabolic"[All Fields] AND "syndrome"[All Fields]) OR "metabolic syndrome"[All Fields]) AND ("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 (clinicaltrial[Filter] OR randomizedcontrolledtrial[Filter])is used as search keywords.

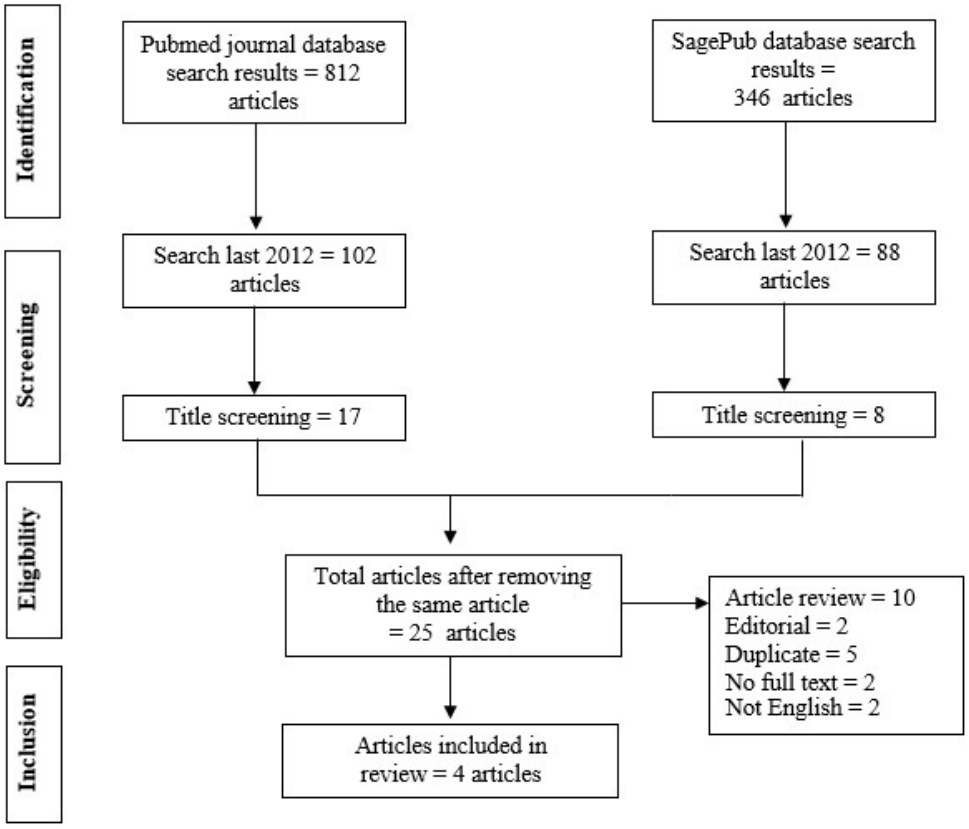

Figure 1. Article search flowchart

Data retrieval

After completing a literature review and reviewing the titles and abstracts of previously published research, the author of the study altered the inclusion and exclusion criteria for the study. The author made this revision after reviewing previously publishedresearch. This was done to determine what should be included and what should not be included in the study. The author made these modifications after conducting a comprehensive examination of other studies provided in previous publications.

During the process of assembling the systematic review, only research studies thatsatisfied each and every criterion were considered significant. These were the only studies considered significant. This action was made in order to ensure that the evaluation is as comprehensive as possible. It is possible to collect information about each individual study, including its title, author, publication date, place of origin, research design, and research variables. This information is available online. This information is capable of being conveyed to the recipient in a variety of formats.

Quality Assessment and Data Synthesis

The authors conducted their own independent reviews of a subset of the researchprovided in the titles and abstracts of the articles in order to identify which studies may be considered. Following this phase, the full texts of the studies that meet the inclusion criteria for the systematic review will be read to determine which research can be used for the review's aims. This will be performed so that the evaluation is as accurate as possible.

RESULT

Patients who had CKD had significantly higher levels of anthropometric data (waist circumference, age, systolic and diastolic blood pressure), serum/plasma data (serum creatinine, serum uric acid, fasting plasma glucose, C-reactive protein, serum triglyceride), urinary and other findings (body mass index, waist-to-hip and waist-to- height ratios, urinary albumin to creatinine ratio, home In models that included and did not include adjustments for diabetes, obesity, and hypertension, metabolic syndrome andat least some of its components were found to be statistically significant risk factors for chronic kidney disease (CKD).[11]

Both being overweight or obese and having metabolic syndrome were associatedwith an increased risk of CKD after adjusting for potential confounding factors; the oddsratios (95% CI) for these conditions were 1.32 (1.15–1.52) and 1.50 (1.31–1.73), respectively. The risk of CKD was found to be 1.31, 1.09–1.57 times in MHO individuals,

1.54 times in MUNO individuals, and 2.05 times higher in MUO individuals when compared to MHNO individuals. There was no significant multiplicative interaction between overweight/obesity and MetS. These connections were somewhat strongeramong people who were older than 60 years old or who had diabetes at the outset.[12]

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Xiao, 2022[11]	China	Cross sectional	1,969	Anthropometric data (waist circumference, age, systolic and diastolic blood pressure), serum/plasma data (serum creatinine, uric acid, fasting plasma glucose, C-reactive protein, serum triglyceride), urinary and other findings (body mass index, waist-to-hip and waist-to-height ratios, urinary albumin to creatinine ratio, homeostasis model assessment of insulin resistance) were significantly higher in patients with CKD ($P < 0.05$). Metabolic syndrome and its components were statistically significant risk factors for CKD in models with and without adjustment for diabetes, obesity, and hypertension.
Wang, 2020[12]	China	Prospective study	15,229	After adjusting for potential confounders, both overweight/obesity and MetS were associated with higher risk of CKD, and the ORs (95% CI) were 1.32 (1.15–1.52) and 1.50 (1.31–1.73), respectively. The risk of CKD was progressively higher in MHO (1.31, 1.09–1.57), MUNO (1.54, 1.22–1.93), and MUO (2.05, 1.73–2.42) as compared with MHNO phenotype, without significant multiplicative interaction between overweight/obesity and MetS ($P_{interaction}$ = 0.906). These associations were slightly stronger among those aged >60 years or with baseline diabetes.
Evangelista, 2018[13]	Korea	Cross sectional	37,002	The incidence of general obesity and abdominal obesity was highest in stage 2 CKD. Stages 3a and 3b were the variables linked with general obesity, and stage 3a was strongly associated with abdominal obesity. The relationship between general obesity/abdominal obesity and CKD decreased in those with advanced stage 4/5 CKD.
Huh, 2017[14]	Korea	Prospective study	10,030	893 participants (14.7%) had CKD after 10 years. After correcting for confounding variables, MS patients had a 1.38 (1.16–1.64) odds ratio (OR) of incident CKD. MS patients had a greater risk of fast eGFR reduction (OR: 1.20, 95% CI: 1.04–1.39). Higher levels of homeostatic model assessment of insulin resistance (HOMA-IR) were related with incidence CKD and fast eGFR decrease irrespective of established CKD risk variables (OR: 1.24, 95% CI: 1.04–1.47).

Other study showed the incidence of general obesity and abdominal obesity was highest in stage 2 CKD. Stages 3a and 3b were the variables linked with general obesity, and stage 3a was strongly associated with abdominal obesity. The relationship between general obesity/abdominal obesity and CKD decreased in those with advanced stage 4/5 CKD.[13] Huh, 2017 showed 14.7% from 893 patient developed CKD. When compared to patients who did not have MS, those with MS had an odds ratio (OR; 95% confidence interval, CI) of incident CKD that ranged from 1.16 to 1.64, and this was determined aftercorrecting for any variables that may have caused a false result.[14]

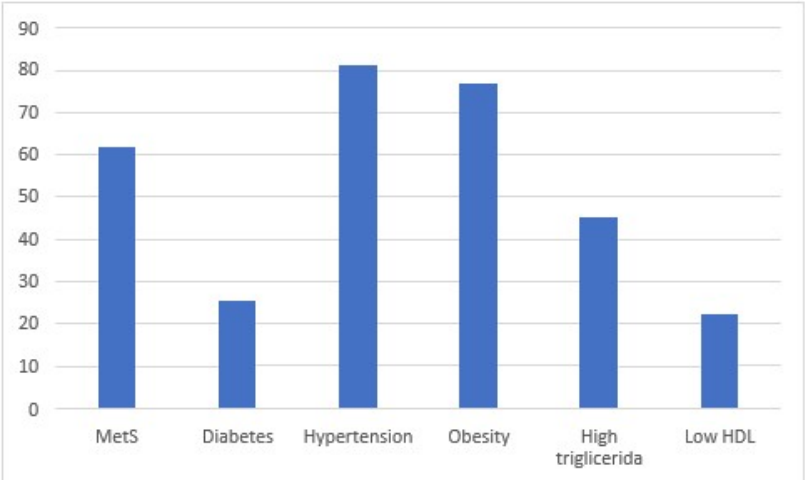

Figure 2. Percentage of components of the metabolic syndrome that cause CKD

The odds ratio for a quick drop in eGFR was 1.20, with a 95% confidence interval ranging from 1.04 to 1.39, greater in patients with multiple sclerosis than in those without the condition. In addition, we discovered that higher levels of homeostatic model assessment of insulin resistance (HOMA-IR) were associated with incident chronic kidney disease (CKD) and rapid decline of estimated glomerular filtration rate (eGFR) independent of traditional risk factors associated with CKD (odds ratio: 1.24, 95% confidence interval: 1.04–1.47).[14]

DISCUSSION

To date, three definitions of MS have been proposed, namely the World Health Organization (WHO), NCEP ATP-III and International Diabetes Federation (IDF) definitions. The three definitions have the same main components with different criteria. Alberti and Zimmet on behalf of WHO presented a definition of SM with its components, including: impaired glucose regulation or diabetes, insulin resistance, hypertension, dyslipidemia with plasma triglycerides >150 mg/dL and/or high density lipoprotein (HDL-C) cholesterol < 35 mg/dL for men or <39 mg/dL for women; central obesity (men: waist-to-hip ratio >0.90; women >0.85) and/or body mass index (BMI) >30 kg/m2; and microalbuminuria (Urea Albumin Excretion Rate >20 mg/min or albumin/creatinine ratio
>30 mg/g).[7,15]

A mechanistic explanation for MetS as a cause of CKD would be more persuasivethan just a connection between the two conditions. It is vital to do research in order to eliminate the "black boxes" that are present along any postulated causal link between metabolic syndrome and chronic kidney disease (CKD).[16] It is possible that there is just one mechanism involved in the progression from metabolic syndrome to chronic kidney disease (CKD), but it is also possible that there are many independent but interdependent processes that are simultaneously at work to bring about severe renal impairment.[17]

It's possible that the processes that cause chronic kidney disease are also the ones that cause metabolic syndrome. In this setting, there may be a "perfect storm" of numerous risk factors leading to increased expression of pro-fibrotic markers. These risk factors include insulin resistance, inflammation, aberrant lipid metabolism, and hypertension. In conclusion, we still are unable to rule out the possibility of chance connections between two otherwise widespread illnesses.[18]

Insulin resistance is likely the most important etiological component associated to MetS that contributes to CKD. Insulin is a hormone that works to reduce inflammation. Insulin resistance is a hallmark of type 2 diabetes. Insulin resistance causes inflammation, which in turn causes oxidative stress and renal insufficiency.[14,19] Increased insulin levels drive the creation of insulin-like growth factor 1 (IGF-1), which in turn causes an increase in connective tissue growth factor, leading to the development of fibrosis in diabetes patients. In addition, and perhaps independently, obesity may lead to an increase in the release of pro-inflammatory cytokines by adipose tissue.[18]

These cytokines include leptin, interleukin-6, and tumor necrosis factor-alpha. It has been shown that leptin can cause an increase in the amount of transforming growth factor beta (TGF-β) that is expressed inside the kidneys, which can result in glomerulosclerosis.[18] Additionally, it may stimulate the formation of type IV collagen. TNF-α may cause the generation of reactive oxygen species (ROS), which may in turn cause malfunction in renal endothelial cells, enlargement of the mesangial tissue, and fibrosis. There is a possibility of a decrease in anti-inflammatory hormones such as adiponectin, which also contributes to insulin resistance.[10,20]

A lack of adiponectin has been linked to an increase in the thickness of the vascular intima as well as the proliferation of smooth muscle cells. It is possible that their vascular benefits do not depend on insulin sensitivity at all, and as a result, they may extend to CKD. In addition, obesity causes an increase in glomerular volume, podocyte hypertrophy, and enlargement of the mesangial matrix prior to the onset of CKD. Triglycerides and free fatty acids may themselves be nephrotoxic because they promote the production of pro-inflammatory cytokines.[19]

Angiotensin II stimulates the production of reactive oxygen species (ROS), which in turn causes a decrease in the production of nitric oxide synthase and renal microvascular injury, as well as ischemia and damage to the tubulointerstitial tissue. Hypertension is another component of the MetS. It is challenging to disentangle the relative contributions of insulin resistance, obesity, and hypertension to these findings vs the MetS syndrome as a whole. In this regard, the presence of early arterial hyalinosis, which is more typical of diabetes but not of MetS, may point towards MetS being a distinct risk factor for CKD independent of its individual components.[21]

This is because arterial hyalinosis is more common in people with diabetes than with MetS. One more hypothesis that may be considered controversial is the idea that hyperuricemia, which is not a "traditional" component of MetS but is associated with MetS, may be a promoter of CKD by inhibiting the production of nitric oxide or even recurrent nephrolithiasis. Another limitation that should be pointed out is that the majority of the mechanistic explanations have been derived from animal models. As a result, the significance of these explanations in human patients with MetS and CKD, who have different lifespans and disease profiles, has yet to be established.[19]

According to several studies, persons who have metabolic syndrome have a 2.5 times increased chance of having chronic kidney disease (CKD). In patients with metabolic syndrome, there is also a twofold rise in the risk of microalbuminuria. In patients with metabolic syndrome, renal impairment typically presents itself years before hypertension or diabetes does.[9,11]

Patients diagnosed with metabolic syndrome are more likely to have the microvascular diseases tubular atrophy, interstitial fibrosis, arterial sclerosis, and global and segmental sclerosis. This is in comparison to healthy controls. Studies suggest that the renal fibrosis seen in patients with MetS may be caused by a constellation of insulin resistance, hypertension, dyslipidemias, and inflammation. This constellation results in a heightened expression of adipocytokines, angiotensin, and inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha.[9,11]

CONCLUSION

According to the information that we have, hypertension is the factor that contributes to metabolic syndrome more frequently than any other, which leads to CKD.

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