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Review Article

Lifestyles and Their Effect on Chronic Kidney Diseases

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Abstract: Chronic kidney disease is a common disease worldwide and a leading cause of global death. It is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 mt2, persisting for 3 months or more, irrespective of the cause. Hypertension and diabetes mellitus are the main risk factors. It is a slowly progressive disease and may lead to an end-stage renal disease requiring dialysis or kidney transplant. It is associated with increased mortality, primarily due to co-morbid cardiovascular disease. CKD can be prevented in many cases. Management includes regular monitoring, control of hypertension, cardiovascular risk reduction, treatment of albuminuria, avoidance of potential nephrotoxins, adjustments in fluid and salt intake, and adequate drug dosing. Several complications such as hyperkalemia, metabolic acidosis, and anemia may occur. Patients with non-dialysis-dependent chronic kidney disease are 10 times more likely to die of cardiovascular diseases than the general population. A decline in GFR of <15 is usually an indication for dialysis. Dialysis-dependent patients are at an even higher risk of dying from cardiovascular complications. The average life expectancy on dialysis is 5-10 years. Kidney transplantation is considered the gold standard treatment in patients affected by end-stage renal disease. It significantly improves the quality of life compared to dialysis. It also improves survival and long-term outcomes in these patients**.** All patients with CKD with a glomerular filtration rate < 30 ml/min/1.73 m^2, and who are expected to reach end-stage kidney disease should be considered for potential future renal transplantation. CKD can be modified by major lifestyle behaviors, which include smoking, alcohol intake, body weight, diet, and exercise. This manuscript discusses the impact of these day-to-day behaviors on CKD.

Keywords: Kidney Diseases, Chronic.

INTRODUCTION

Chronic kidney disease (CKD) is a common disease [1, 2]. It is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73 mt^2, persisting for 3 months or more, irrespective of the cause [3]. CKD has an estimated worldwide prevalence of 10.6%-13.4%, and its prevalence is growing rapidly [4]. However, less than 5% of patients with early CKD report awareness of their disease [5]. In 2017, CKD affected almost 700 million people in the world [4]. Its prevalence is more in low- and middle-income than in high-income countries [6]. Those affected with CKD exceed those with diabetes, osteoarthritis, COPD, asthma, or depressive disorders [7]. CKD is slowly progressive leading to irreversible nephron loss and end-stage renal disease (ESRD)(eGFR<15ml/min), requiring dialysis or kidney transplant, leading to premature death [8, 9]. It is estimated that the number of people requiring renal replacement will double to 5.4 million by the year 2030 [10]. Hypertension and diabetes mellitus are the main etiological causes [11-13]. In addition to the lifestyle factors discussed in this manuscript, sickle cell anemia [14] and genetic factors [15] may also play a role in its causation. Usage of nephrotoxic drugs is sometimes responsible [16]. CKD patients experience considerable complications [17] including those involving the cardiovascular system [18], cognition [19], hyperkalemia [20], metabolic acidosis [21], hyperphosphatemia [22], vitamin D deficiency [23], secondary hyperparathyroidism [24], and anemia [25]. CKD also leads to frequent hospitalization [26]. It is associated with a lower quality of life [27] and premature death [28]. CKD individuals have a mortality rate that is over 100-fold compared to that seen in the normal population [29]. CKD results in more deaths than tuberculosis or HIV and is presently ranked as the 12th leading cause of death out of 133 conditions in the

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world [7]. The major cause of mortality in CKD is due to lethal cardiovascular events [29].

DISCUSSION

Five healthy lifestyles have been recognized as having a major impact on morbidity and mortality [30]. These behaviors are non-smoking, abstinence or low to moderate alcohol intake, a normal body mass index, regular exercise, and a prudent quality of diet [30]. According to Yanping et al. adherence to these lifestyles and greatly improve survival and provide several extra years of life, both in men and women [30]. Smoking is the leading preventable cause of death worldwide[31].Tobacco smoke is full of toxic chemicals, and many of them are carcinogenic [32]. Alcohol is protective for some diseases if it is taken in moderation [33] –however, heavy drinking (intake, of >60 g/day in men and >40 g/day in women), is harmful to health [34]. Obesity is described as having a BMI >30kg/m^2 [35]. It is prevalent all over the world [36]. Abdominal obesity is also of concern, as when compared with subcutaneous fat, the white visceral fat secretes harmful free fatty acids and adipocytokines [37]. A sedentary lifestyle is also harmful [38]. The World Health Organization recommends that adults should accumulate at least 150 min of moderate-intensity physical exercise per week and young people aged 5–17 years should accumulate at least 60 min of daily physical exercise of moderate to vigorous intensity [39]. Diet also plays an important role in health and disease [40]. The dietary guidelines for Americans recommend that the diet be well balanced, mostly plant-based, rich in fruits and vegetables, whole grains, fish, low in sugar and salt, and with the occasional intake of lean meats [41]. It should limit or eliminate trans-fats, saturated fats, fried foods, sodium, red meat, refined carbohydrates, and sugar-sweetened beverages [41]. These five lifestyles and their impact on renal diseases are discussed below:

Smoking

Tobacco smoking damages the kidneys [42-44]. It is associated with the presence of proteinuria and impaired kidney function [43, 45]. In a recent analysis of 15 prospective cohort studies involving 65,064 incident CKD cases, Xia *et al*. confirmed the increased risk of CKD in smokers when compared with nonsmokers [46]. Continuing smoking also accelerates the progression of established CKD [47] and accelerates death [48]. Among smokers, mortality due to renal failure was increased by 2-fold, and death due to essential hypertension and hypertensive renal disease was increased by 2.4- to 2.6-fold [48]. Smoking cessation reduces the risk of incident CKD [49], as well as its progression [50]. Smoking is also known to increase the risk for kidney cancer in CKD patients [51]. Exposure to secondhand smoke also increases incident CKD [52]. Smoking cessation reduces the incidence [53] as well as progression of CKD [54]. Smoking cessation for ≥ 20 years was associated with a lower risk of incident CKD among former smokers [53]. Smoking cessation decreases proteinuria in patients with CKD and slows the progression to ESRD [54]. The adverse kidney outcomes are attenuated as the duration of smoking cessation increases [55]. Smoking is associated with atherosclerotic vascular disease, a major cardiovascular risk factor [56, 57]. Smoking is also associated with metabolic syndrome, a known risk factor for chronic kidney disease [58]. Smoking thus acts as a risk amplifier in these patients [59].

Alcohol

Alcohol is consumed occasionally or daily by approximately 20–36% of patients with CKD [60, 61]. Several studies show that low to moderate intake may be safe in these patients [62, 63], and may even reduce the risk of ESRD [63]. Li *et al*. in a recent meta-analysis of prospective cohorts concluded that even high amounts of alcohol use may be associated with a lower risk of incident CKD or ESRD [64]. A recent study concluded that all levels of alcohol intake were CKD protective [65]. This study was a meta-analysis of 25 eligible prospective cohort studies, including 514,148 participants and 35,585 incident CKD cases, and showed that light (<12 g/day), moderate (12-24 g/day), and heavy (>24 g/day) alcohol consumption is protective against chronic kidney disease in adult participants especially in males [65]. However, some studies, including two Mendelian randomization studies, indicate that heavy alcohol consumption or chronic alcohol consumption is positively associated with an increased risk of end-stage kidney disease [66-68]. Mechanisms of alcohol-induced kidney damage include potential oxidative stress injury, increase in blood pressure, and activation of the renin-angiotensin-aldosterone pathway [69-71]. Alcohol's relationship with kidney disease is therefore controversial – however, it is generally accepted that low to moderate alcohol intake is overall safe in CKD patients [72, 73]. This is because alcohol helps cardiovascular diseases [72] and lowers the risk of DM [73]. Cardiovascular events are common cause of morbidity and mortality in CKD patients [29], and DM is a major cause of CKD [13]. Since alcohol consumption can lead to significant problems, nondrinkers should not start drinking for any potential benefit [74].

Obesity

Obesity is also causally related to CKD [75, 76]. Overweight and obesity increase the risk of CKD – Risk Ratio of 1.40 and 1.83 respectively [77].. Higher body mass index (BMI) is associated with the presence of proteinuria in individuals without kidney disease [78, 79]. Furthermore, in numerous large population-based studies, higher BMI appears associated with the presence and development of low estimated eGFR[80], with more rapid loss of estimated GFR over time [81], and with the increased incidence of ESRD[82]. Class II obesity (BMI 35-39.9) and above, has been associated with more rapid progression of

CKD in patients with pre-existing CKD [83]. Obese patients have a higher risk of complications during and after renal transplantation surgery [84]. Visceral obesity or a waist circumference (WC) >102 cm and a waist-hip ratio (WHR) of 0.9 in females, and a WC >88 cm and WHR >0.8 in males, is associated with an increased risk of CKD, even if the BMI is normal [85-88]. Higher visceral adipose tissue measured by computed tomography has been associated with a higher prevalence of albuminuria in men [89]. The observation of a BMI-independent association between abdominal obesity and poorer renal outcomes is also described in relationship with a kidney transplant [90], and mortality in patients with ESRD [91], suggesting a direct role of visceral adiposity. Obese patients have a higher risk of complications during and after renal transplantation surgery [92]. Weight loss helps improve kidney function [93, 94]. In obesity-related glomerulopathy, a weight loss of 12% resulted in a decrease in proteinuria by >80% [93]. Weight loss with bariatric surgery also results in an improvement in kidney function [94]. An association between obesity and nephrolithiasis has also been described, particularly with uric acid and calcium oxalate calculi [95, 96]. Obesity is also associated with an increased risk of cancer of the kidney [97, 98]. In a meta-analysis, Guh *et al*. in 2009, estimated that this increased risk was 1.82 for men and 2.64 for women [97]. In a population-based study with 5.24 million individuals, from the United Kingdom and published in 2014, a 5 kg/m^2 higher BMI was associated with a 25% higher risk of kidney cancers [98]. Obesity impacts the kidneys via several mechanisms [99-106]. These include more inflammatory cytokines, increased oxidative stress, abnormal lipid metabolism, activation of the renin-angiotensin-aldosterone system, and insulin resistance [99-103]. There may be a direct pressure effect of the increased perirenal fat also [104]. Obesity is also closely associated with type 2 diabetes mellitus (DM) and hypertension (HTN), which are also major risk factors for CKD [105,106]. Despite the deleterious effects of obesity on CKD and its progression, several studies have noted that obesity may result in lower mortality rates in patients with advanced CKD and end-stage renal disease [107, 108]. Obesity may provide survival benefits because of associated better protein and energy reserves, a higher muscle mass with enhanced antioxidant capacity, and lower circulating actin and higher plasma gelsolin levels – these helps protect against cachexia and muscle wasting [109, 110].

Exercise

Exercise is beneficial in reducing the risk of CKD and slowing the decline in eGFR in patients with established CKD [111,112]. Highly active individuals, when compared to inactive individuals, (Second National Health and Nutritional Examination Survey) have a reduced risk for developing CKD [113]. In a prospective analysis of the Cardiovascular Health Study, greater baseline physical activity was associated with a lower risk of eGFR decline >3 mL/min/1.73 m^2 per year [114]. A recent study has also confirmed the preventive benefits of exercise in CKD [115]. Exercise in patients with established CKD is associated with not only a slower decline in eGFR but often an improvement [116, 117]. Greenwood *et al*. in a retrospective longitudinal cohort study estimated that each extra hour of sedentary behavior was associated with a worsening of kidney function, while each extra hour of total physical activity was associated with a better kidney function [117]. In a meta-analysis of 13 randomized controlled trials totaling 421 patients with CKD, Zhang *et al*. concluded that exercise therapy was associated with a +2.6 mL/min increase in eGFR [118]. Exercise training in dialysis patients prevents muscle atrophy and improves functional capacity and quality of life [119, 120]. Benefits of exercise have also been noted in renal transplant patients [121]. Exercise in CKD patients results in a better prognosis, an improved quality of life, and increased survival [122-124]. There is a reduction in adverse cardiovascular outcomes [125]. Exercise has been recommended for CKD patients by major kidney organizations [126-128]. Exercise is usually feasible, and well-tolerated in CKD patients, including those on dialysis and those following renal transplantation [129-131]. Physical activity decreases inflammation and favorably modulates endothelial function, the renin-angiotensin system, and renal sympathetic nerve activity [132-134]. Exercise also reduces several risk factors for CKD, such as DM blood pressure, adiposity, and dyslipidemia [135-138].

Diet

Diet plays an important role in CKD – not only to prevent the disease/slow down the progression and potential complications but also to decrease the effects of its main causes and comorbid conditions [139]. Patients adhering to a Mediterranean diet for six years have a 50% lower risk of developing CKD140 as well as reduced cardiovascular disease (CVD) complications in these patients [141]. Dietary Approaches to Stop Hypertension Dietary (DASH) diet also has an inverse relationship with CKD [142-144]. Poor adherence to the DASH diet is associated with a 16% higher risk of CKD (a study of 15,000 Atherosclerosis Risk in Communities participants) [145]. A diet high in fruits and vegetables results in a slower CKD progression and reduces complications and is associated with decreased mortality [146]. A dietary pattern, besides being rich in fruits and vegetables, and rich in whole grains, and low-fat dairy foods is associated with lower urinary albumin to creatinine ratio [147]. A primarily plant-based diet leads to a 12% lower risk of eGFR decline a higher eGFR, and improved serum albumin levels [148,149]. Individual dietary components of a plant-based diet influence blood pressure, lipid levels, oxidative stress, insulin sensitivity, systemic inflammatory responses, pro-fibrotic processes, thrombosis risk, and endothelial function in these patients, beneficially modulating the clinical outcomes [150-152]. Plant-based diets also are associated with a better quality of life and decreased

mortality in adults with CKD [153]. A diet rich in animal protein is potentially harmful to CKD patients [154]. Animal protein (red and processed meat), results in higher blood pressure, vasodilation of afferent renal arterioles, glomerular hypertension, hyperfiltration, metabolic acidosis, mitochondrial oxidative stress, DNA damage, and increased accumulation of the end-products of protein catabolism [154]. CKD patients may be advised to reduce their fluid and salt intake and even curtail their protein intake, depending on the clinical situation [155-157]. A healthy diet may prevent >90% cases of DM and 65% of cases of HTN - the main causes of CKD [158, 159]. Further, a CKD patient may not live enough to require dialysis, as CKD has a 2-fold higher prevalence of CVD and may succumb earlier, because of a heart attack or stroke [160]. Mortality is high in CKD, primarily from cardiovascular complications [161, 162]. A healthy diet will also help mitigate CVDs in these patients.

CONCLUSION

Chronic kidney disease affects 8% to 16% of the population worldwide and is a leading cause of death. It is associated with significant complications like fluid retention, hypertension, metabolic acidosis, and anemia. It may gradually progress to end-stage renal disease, requiring dialysis or renal transplantation. It is associated with increased mortality. Cardiovascular diseases are the major cause of death in these patients. Optimal management, therefore, includes reduction of cardiovascular risk. Monitoring is also required for albuminuria, hyperkalemia, and other metabolic abnormalities. Prevention, early detection, and treatment are therefore extremely important. Healthy lifestyles play an important role during all stages of CKD. Besides CKD, other renal ailments like nephrolithiasis, and kidney cancer, are also associated with unhealthy lifestyles. The latter leads to excess morbidity and mortality in these individuals. There are also excess costs to individuals and the entire society. Healthy lifestyles play an important in reducing the burden of CKD worldwide.

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