Chapter 7

Chronic Kidney Disease

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1 Introduction

In 2018, chronic kidney disease (CKD) was estimated to affect approximately 850 million people worldwide. Up to 10.5 million patients worldwide with CKD need dialysis or a kidney transplant, although many patients cannot receive these lifesaving treatments because of high costs or lack of resources [1]. CKD has emerged as one of the highest-occurring, life-threatening, non-communicable diseases in both developing and developed countries.

As of December 31, 2017, there were 334,505 patients undergoing dialysis in Japan, an increase of 40,959 from January 2017. With the increasing number of new dialysis patients, the medical costs associated with this procedure now exceed 1 trillion yen annually [2]. Therefore, the Ministry of Health, Labour and Welfare (MHLW) is aiming to improve the care and outcomes for patients with kidney disease in Japan through the early detection of CKD and adequate standardized treatments. The MHLW set a goal of reducing the number of new dialysis patients to less than 35,000 by 2028 [3].

CKD is defined as kidney damage/injury for ≥ 3 months and/or a glomerular filtration rate (GFR) < 60 mL/min per 1.73 m² for ≥ 3 months with or without kidney damage [4]. Socioeconomic status (SES) has been reported to be associated with the

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K. Kondo (ed.), *Social Determinants of Health in Non-communicable Diseases*,
Springer Series on Epidemiology and Public Health,
https://doi.org/10.1007/978-981-15-1831-7_7

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onset of CKD [5–11]. In addition, individuals with lower SES may suffer from unrecognized and untreated CKD as well as end-stage renal disease [5, 6].

Zeng et al. [5] and Vart et al. [6] performed meta-analyses to explore the association between SES and CKD. However, their meta-analyses did not include results in Japan. We explored the relationship between SES and CKD in other countries as well as in Japan and discuss factors related to the future direction of prevention measures for CKD.

2 Methods

2.1 *Countries Other than Japan*

Studies that measured the association between SES and CKD were systematically identified from PubMed. Studies published in English from the inception date of the database to June 2018 were retrieved. Keywords included “socioeconomic status,” “income,” “education level,” “occupation,” “chronic kidney disease,” “chronic renal failure,” and “dialysis.” Abstracts without full articles were excluded. The search yielded 71 articles.

2.2 *Japan*

Suitable studies that measured the association between SES and CKD were systematically identified from PubMed. Studies published from the inception date of the database to June 2018 were retrieved. Keywords included “socioeconomic status,” “income,” “education level,” “occupation,” “chronic kidney disease,” “chronic renal failure,” “Japan,” and “Japanese.” Abstracts without full articles were excluded. The search yielded two articles. Moreover, Japanese studies that measured the association between SES and CKD were identified from the Japan Medical Abstracts Society. As a result of the search, there were no original articles; however, two abstracts were identified.

3 Results

3.1 *Countries Other than Japan: Factors Associated with CKD*

3.1.1 *SES Status*

Studies have compared different low SES areas and showed a higher incidence and worse prognosis of CKD among subjects living in the most deprived areas [5, 7–9]. A retrospective cohort study in Southampton and South-West Hampshire Health

Authority, United Kingdom (CKD incidence rate, 1701/100,000 persons per year) [7] examined the incidence of CKD in several low SES areas. Results showed that people living in the most deprived area had an approximately 40% higher incidence of CKD than those in other low SES areas. In another survey [8] in the United Kingdom, among five lower SES areas, the lowest rated area had the highest number of patients with CKD (19,599 patients per million population). In addition, living in the lowest SES quintile area (most deprived area) as compared with the highest SES area (least deprived area) was associated with a greater risk for a lower estimated glomerular filtration rate (eGFR). This study also analyzed the risk for progressive CKD among 1657 patients according to the SES of their area of residence. The risk for progressive CKD was 6.7 times higher among men and 9.8 times higher among women from the lowest SES area than for CKD patients from the highest SES area. Moreover, a cohort study from the United States that examined 12,856 participants [9] found that living in the lowest SES quartile was associated with more than twice the risk for progressive CKD compared with living in the highest quartile.

3.1.2 Income

A cohort study of 14,086 participants [10] in the United States reported that the hazard ratio (HR) for incident CKD was 1.10 [95% confidence interval (CI) 1.01–1.20] in a middle-income group (\$12,000–24,999) and 1.30 (95% CI, 1.17–1.44) in a low-income group (<\$12,000), with a high annual household income (≥\$25,000) as reference. In a cohort study of 4735 participants in the United States [11], the HR for risk of progressive CKD among lower-income individuals (<\$12,000) was 1.4 (95% CI, 1.0–1.9) compared with higher-income individuals (≥\$35,000).

3.1.3 Education

A cohort study of 14,086 participants [10] reported that the HR for incident CKD was 1.09 (95% CI, 1.01–1.18) in the middle-education level group (high school/equivalent) and 1.32 (95%CI, 1.20–1.45) in the low-education level group (<high school), using the high education level (>high school) as a reference. In a population-based case-control study of 1924 participants in Sweden, Fored et al. [12] demonstrated that the odds ratio (OR) for risk of CKD among subjects with 9 years or less of schooling was 1.3 (95% CI, 1.0–1.7) relative to those who went to university. In a study of 60,202 individuals in Brazil [13], it was reported that a higher occurrence of CKD was observed among individuals with a lower education (illiterate/elementary education incomplete) relative to those with higher education (higher education complete) (prevalence ratio 1.65; 95% CI, 1.10–2.46).

3.1.4 Occupation

Fored et al. [12] demonstrated that the OR of CKD among unskilled manual workers was 1.72 (95% CI, 1.2–2.5) relative to professionals. In addition, they showed that among patients in the unskilled manual workers group, 27% had a GFR in the lowest quartile, 24% in the second quartile, 27% in the third quartile, and 21% had a GFR in the highest quartile. A cross-sectional study in the United Kingdom showed that lower occupational grade (clerical and support staff) was associated with a greater OR for decreased eGFR (OR 1.31; 95% CI, 1.12–1.53) [14].

3.2 *Factors Associated with CKD in Japan*

3.2.1 SES Status

We could not find any original articles from Japan that reported the relationship between SES and CKD by living area.

3.2.2 Income

Takagi et al. [15] examined the relation between SES and mortality risk in 456 patients undergoing hemodialysis (HD). They found that patients undergoing HD from households with an annual income <two million yen had a mortality risk that was 2.19 times higher than patients from households with an annual income of $\geq$ two million yen. In a study using data from the National Health and Nutrition Examination Survey in Japan, there were more people with CKD in low-income groups than in the higher-income group [16].

3.2.3 Education

Imanishi et al. [17] investigated the influences of education level on mortality and hospitalization among 7974 patients undergoing maintenance HD in Japan. They reported that patients with less than a high school education and patients who graduated high school with some college tended to have elevated mortality when compared with patients who graduated from university.

3.2.4 Occupation

We could not find any original articles from Japan that reported the relationship between occupational stratification and CKD.

4 Discussion

4.1 *Relation of SES and Lifestyle with CKD*

The incidence of CKD is closely related to unhealthy lifestyle behaviors, such as smoking, lack of exercise, and unhealthy eating styles [18–22]. According to Cockerham [23], lifestyle is fundamentally constrained by social hierarchy and an individual's living conditions. Health-related lifestyles related to SES for both individual and regional-level characteristics have been considered in some previous studies and different results have been reported [24, 25].

4.1.1 Smoking

Cigarette smoking is associated with an elevated risk for incident CKD/end-stage renal disease in the adult general population [18, 22]. Tobacco smoke is a major source of adult exposure to cadmium, and smoking contributes more to cadmium body burden than does the typical diet [26]. Cadmium is directly nephrotoxic and can induce renal tubular damage and a progressive reduction in eGFR [27]. Urine cadmium is an indicator of kidney and body burden, and the kidney is a critical target for cadmium toxicity, with renal tubular and glomerular damage manifested by proteinuria and progressive decreases in GFR, respectively [28]. There is also evidence that smoking is associated with many individual-level SES indicators, such as income, education, and occupation, and smoking is more frequent among socioeconomically disadvantaged people [29–31].

Smoking may be more common in people with a low SES for several reasons. First, smoking may serve as a coping mechanism that helps people deal with the different and stressful aspects of their daily lives. Lower family income was associated with higher severe uncertainty stress (OR 1.25; 95% CI, 1.06–1.49) [32]. Both men and women with low SES were shown to experience more stress than those with high SES [33]. Second, people with low SES may be less knowledgeable with regard to information and resources for healthy behavior. Furuya et al. [34] reported that health literacy scores of low-SES people were low. People with low SES have been shown to be less knowledgeable about the harmful effects of smoking [29].

Among studies in Japan, Yun et al. [30] indicated that the lowest household income group had a higher risk for smoking than the highest household income group in both men and women. A study of 32,981 older people in Japan observed smoking rates of 23.6% in men and 4.7% in women for those with less than 6 years of education and 18.9% in men and 1.9% in women for those with ≥ 13 years of education [31].

4.1.2 Exercise

A lack of habitual exercise is an independent risk factor for CKD [35]. Exercise has many different health-related parameters in CKD. Exercise training is effective in combating muscle atrophy associated with CKD through upregulation of protein synthesis, increasing muscle mitochondria content, and reducing muscle catabolism [36]. Physical activity also counteracts many of the metabolic disturbances that promote the progression of CKD [37]. It has been shown that exercise habits are also related to SES [24, 25, 33, 38]. Participants with a higher educational level are more likely to be physically active and involved in sports [38]. Several points may explain the lower exercise habits among people with lower SES. First, environmental barriers, such as neighborhood safety or inadequate street lighting, may directly and indirectly undermine exercise habits [39, 40]. Lack of parks and low-cost exercise facilities in lower SES areas may also contribute to these findings. Second, it is possible that the low-SES group spends more time watching television than the high-SES group. Andrade-Gómez et al. [41] indicated that television watching time was greater in those with a lower education. Increased time watching television, a passive and sedentary activity, may be associated with less recreational physical activity. Data on 32,981 elderly people in Japan also found that both men and women of low SES were more likely to walk <30 min/day. This finding was true for 47.3% of men with <6 years of education compared with 33.9% of men with ≥ 13 years of education [33].

4.1.3 Diet

The association between dietary macronutrients, especially protein intake, and the incidence and progression of kidney disease has been examined in multiple clinical trials [42]. Managing proper protein intake remains one of the most important modifiable lifestyle factors in the progression of kidney disease to CKD. More severe protein restriction (<0.3 g/kg per day) reduces the decline in GFR [43]. Furthermore, high salt intake has been related to the development of CKD [44]. In addition, high intake of fresh fruit, vegetables, fish, and unsaturated fats (mainly olive oil) is associated with a lower prevalence of CKD [45]. Several factors contributed to findings related to dietary habits and CKD. Poor eating habits are commonly found in people with low SES, partly because healthy diets are more expensive. Drewnowski et al. [46] demonstrated that higher consumption of fruit, vegetables, meats, and fish was associated with higher costs. In contrast, higher consumption of fats and oils, added sugars, and refined grains was associated with much lower costs. People of low SES may not be able to afford a healthy diet and thus tend to consume foods of lower nutritional value and lower quality. Second, people with less education may lack knowledge regarding healthy dietary patterns. Kuczmarski et al. [47] indicated that the relationship between health literacy and diet quality became stronger as the education level increased. Eating habits have also been reported to be related to SES in other studies [25, 46–49]. Daily consumption of fruits, vegetables, milk, meat,

rice, fiber, fish, and dairy products was shown to be lower in people with low SES than those with high SES; those with a lower SES show a higher daily consumption of cakes, salty/fatty snacks, sweet drinks, fast foods, and potatoes [25, 48]. Moreover, Li et al. [49] reported that the highest prevalence of low fruit and vegetable consumption was observed among those aged ≥ 65 years and those who were illiterate or only had a primary school education.

4.2 *Relation Between SES and Life Course in CKD*

Previous studies have reported that adverse SES in adulthood is associated with adult CKD [50, 51]. The life-course perspective essentially reflects the study of long-term protective and risk factor effects of physical and social exposures from gestation through adult life, which may also reflect the incidence of CKD. That is, childhood SES may be related to the onset of CKD in adulthood.

Low birth weight (LBW) is strongly associated with childhood-onset CKD [52]. Brenner et al. [53] proposed that LBW may be associated with a congenital deficit in the number of nephrons, which would lead to a predisposition to reduced renal sodium excretion. Moreover, LBW can be attributed to intrauterine growth restriction (IUGR; birth weight less than the tenth percentile for gestational age) or premature birth. LBW associated with IUGR has a stronger association with adult CKD [54], and increased prevalence of microalbuminuria, proteinuria, and lower GFR are seen among adults who had LBW [55, 56]. Shoham et al. [51] reported that salient risk factors and markers that are associated with both SES and CKD early in life include diet and birth weight. Previous studies indicated that many infants of mothers with low SES had LBW [57–59]. Rammohan et al. [57] demonstrated that babies born to women with low family income were significantly more likely to have LBW than those born to women with medium family income (OR, 5.09; 95% CI 1.59–16.32) or high income (OR, 2.29; 95% CI, 0.82–6.38), while Yaya et al. [58] reported that compared to those who had higher education, the OR of experiencing LBW babies was 1.73 and 1.56 for those below the primary and secondary education levels, respectively.

Similarly, maternal diversity of nutritional intake before and during pregnancy is a critical factor influencing birth weight [59]. LBW was linked to poor diet, and poor diet is associated with low SES [57, 60]. Low education and income are considered a reason for LBW, which occurs frequently in low SES people. Lee et al. [60] indicated that women with high SES were more likely to consume healthier food and had better opportunities to maintain dietary profiles consistent with nutritional recommendations or dietary guidelines. Rammohan et al. [57] reported that a low diversity of foods was more common in the diets of women with less education/less income. Similarly, babies born to women with low family income were significantly more likely to have LBW than those born to women with medium family income (OR, 5.09; 95% CI; 1.59–16.32) or high income (OR, 2.29; 95% CI 0.82–6.38) [57]. It is possible that low maternal dietary diversity is caused by a lack

of dietary knowledge. Kim et al. [61] reported that the consumption of fruit, vegetables, red meat, and milk was significantly higher in subjects with a higher education level. Another study supported the finding that people with a high education tend to have better dietary intake than people with a low education [62]. O'Brien et al. [63] reported that during pregnancy, a dietary education session was not effective among less educated women.

It is suggested that the low SES of parents leads to LBW in infants and increases the risk for developing adulthood CKD. In Japan, the proportion of LBW infants is increasing. According to the MHLW, the weight of LBW in infants has dropped 200 g in the past 40 years [64]. In the future, these children may have an increased risk of CKD.

5 Summary

We demonstrated that low SES is related to the onset and progression of CKD. Moreover, we found that low SES of parents is associated with an increased risk for developing CKD in children. There are approximately 13.3 million Japanese patients with CKD [3], and this number increases every year. The number of patients who ultimately need dialysis is also increasing and approximately 330,000 Japanese are undergoing HD [2]. There are few reports on the association between Japanese CKD patients and SES. However, it is reported that there are many patients of low SES that are undergoing HD and experiencing CKD. Because SES is strongly correlated with the onset and progression of CKD, it is likely that standard approaches to promoting improvements in individual lifestyle habits alone will not be effective. Therefore, the MHLW must consider the development of programs that target low SES citizens to educate them about CKD and address unhealthy lifestyle behaviors such as smoking, lack of exercise, and unhealthy eating styles.

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