A Comprehensive Public Health Approach to Address the Burden of Renal Disease in Singapore

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Abstract. With the epidemic rise of ESRD in multiple regions of the world, there is an urgent need to implement programs to address this increasing burden of kidney disease. We illustrate a public health approach using the program of the National Kidney Foundation of Singapore that incorporates stepwise primary, secondary, and tertiary strategies for prevention. Components of the program include an aggressive public education program, routine surveillance for kidney disease and associated chronic diseases, the implementation of a disease management program to improve physician practice patterns, and the provision of comprehensive services in the community through a network of Prevention Centers designed to optimize the care of patients at risk for kidney disease. Finally, an equally important aspect is the clinical and epidemiologic research component, because this will provide clear benchmarks to determine the program’s effect on ESRD as well as generate information that can be used to identify future directions for this evolving program.

The rising annual incidence of ESRD in many countries of the world (1), its profound effect on morbidity and mortality, and the escalating health care costs associated with it have promoted the development of strategies aimed at preventing the development and progression of chronic kidney disease (CKD). These include population-based and high risk screening programs (2,3), the initiation of public education campaigns targeted at improving public awareness of kidney disease and its consequences (4), and the dissemination of evidence-based guidelines for the approach to CKD (5). Current clinical recommendations for several components of kidney disease prevention are based on consensus expert opinion rather than on clinical trial data (5). In addition, many of these programs are in the early stages of implementation and thus, the cumulative effectiveness of these independent interventions remains to be seen. Similarly, in Singapore, a program for the prevention of kidney failure is still in its infancy. Nevertheless, given its integrated public health and community-based approach, with components of screening, early detection, and early intervention, as well as the country’s small size and unique logistical and demographic advantages, the NKF Singapore Prevention Program merits consideration.

The National Kidney Foundation Singapore (NKFS), the largest charitable organization in the country, is responsible for providing subsidized dialysis care to over 60% of the country’s total ESRD population (6). The Prevention Program, components of which were initiated in 1997, has a long-term goal of effecting a plateau in the rising incidence of ESRD in the country based on a framework of the natural history of kidney disease development and progression. It incorporates stepwise primary, secondary, and tertiary prevention approaches to intervene at various stages of kidney disease and associated chronic diseases, including type 2 diabetes mellitus and hypertension (7). This report describes this comprehensive strategy of screening, early intervention, research, and improved care of individuals at risk for the development of kidney disease and provides evidence of the efficacy of the surveillance components of this integrated strategy.

Surveillance and Early Detection

Although data on clinical efficacy of screening for kidney disease are limited, existing clinical guidelines for CKD espouse screening strategies for high-risk populations (5). These recommendations are generally extrapolated from the efficacy of early intervention in specific clinical settings, such as the screening for the early stages of diabetic nephropathy (5). Similarly, the NKFS incorporates such a high risk screening strategy but has initiated a population-based component as well. In the NKFS program, the primary prevention component is more akin to a surveillance system, given its broader aims that may affect populations, rather than specific individuals (8).

The objectives of the Primary Prevention Program include (1) the identification of individuals and population groups that may benefit from further treatment, specific prevention approaches, or targeted educational programs, (2) the determination of the prevalence of risk factors and the identification of novel risk factors in the unique multicultural population of Singapore, and (3) the consolidation of screening data to guide the secondary and tertiary public health prevention programs of the NKFS.

Epidemiologic Basis for Screening for Renal Disease. Several general considerations are used in determining the value of a screening program for renal disease. These include:
(1) a significant prevalence of renal disease in the population; (2) a considerable proportion of the population with preclinical or asymptomatic disease; (3) an acceptable screening test that is reliable and accurate; (4) early detection through screening leads to effective treatment that results in improved outcomes when compared with an unscreened population; and (5) a cost that is considered reasonable as measured by the benefit achieved by screening and early intervention (9,10). An extensive review of each criterion is beyond the scope of this manuscript. However, a limited discussion is relevant as a background for the NKFS Screening Program.

There is no doubt that the burden of CKD is significant in the United States. National Health and Nutrition Examination Surveys (NHANES) III data reveal that an estimated 19.5 million Americans, representing 10.9% of the population, have stage 1 or higher CKD (11) based on the Kidney Disease Outcome Quality Initiative (K/DOQI) classification of stages of CKD (5). Furthermore, 8.3 million Americans, or 4.6% of the population, are estimated to have significant reduction in kidney function as defined by a GFR below 60 ml/min per 1.73 m² (11). Given the large number of Americans with some degree of clinically documented CKD, it is reasonable to assume that a significant percentage of the US population has undetected CKD. Furthermore, limited analysis on subpopulations with chronic diseases that lead to CKD suggest an underdetection and undertreatment of kidney disease in patients with diabetes mellitus or hypertension (12). Whether similar rates of undetected kidney disease are present in the Asian population is unknown, and identifying these rates is one of the objectives of the NKFS prevention program.

Appropriate screening tests for CKD include the detection of macroalbuminuria through standard dipstick testing or quantitation through an albumin to creatinine ratio, detection of microalbuminuria through specialized dipstick testing, and an estimation of GFR through accepted equations based on serum creatinine (5). It is beyond the scope of this manuscript to review data regarding the reliability and accuracy of these screening tests. However, both the American Diabetes Association and the USNKF also support the use of standard urinary dipsticks for screening of albuminuria, with subsequent quantitation using either a spot or timed urine collection (13,14). The ability of these screening tools to detect CKD has not been systematically analyzed for their sensitivity and specificity for predicting eventual ESRD. However, in a study evaluating the relationship between a single random dipstick proteinuria and albumin to creatinine ratios, there was a 91% positive predictive value of ≥1+ dipstick proteinuria for clinically significant quantitated proteinuria in both diabetic and nondiabetic populations (15). Furthermore, a single episode of dipstick positive proteinuria was found to be a significant predictor for all-cause, as well as cardiovascular mortality (16). Taken together, these studies support the value of screening by dipstick proteinuria in the early detection of CKD and its complications.

Early detection of kidney disease and subsequent treatment associated with significant reduction of proteinuria have been demonstrated to result in markedly improved renal and cardiovascular outcomes (17,18). Indeed, numerous large scale clinical trials including the REIN study (19), and the AIPRD study (20), among others, demonstrated renoprotection and renal function stabilization, particularly with the use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers, independent of their BP-lowering effect.

Perhaps one of the most relevant criteria for screening for kidney disease that is supported by the least amount of published data or analysis is whether population-based or high-risk screening is within the range considered to be cost-effective. Indeed, in a recent review of cost-effectiveness of screening programs, the majority of which were for diabetic renal disease (21), it was the treatment of all patients with diabetes with ACE inhibitors that was considered to be most cost-effective (22). Furthermore, in the only analysis on nondiabetic kidney disease, simulation models for cost-effectiveness analysis suggest that a single opportunistic dipstick screening for older individuals proves to be cost-saving (23). Thus, although clinical trial data on the cost-effectiveness of screening for kidney disease are lacking, simulation models demonstrate a role for screening and early treatment of CKD.

Altogether, some data appear to argue for the role of screening for CKD. With these in mind, the NKFS developed and implemented a nationwide screening program for proteinuria and other associated risk factors for renal disease.

**Materials and Methods.** Both population-based and high-risk prevention strategies were incorporated in the NKFS screening program. Although the high-risk strategy is the preferential option of other existing programs (3), largely as a result of its perceived cost-effectiveness, the population-based strategy is believed to have a larger effect on diseases for which population behavior characteristics play a major role (7,24,25). At the NKFS, both population-based and high-risk strategies were incorporated into its primary prevention and early detection programs. Its components include nationwide public education and population-based screening.

The NKFS Public Education campaign takes into account unique differences in age and racial subgroups. From health talks to students, teachers, and the general community, to the development of health brochures, creation of health fairs, design of a health education website, and the production of a television drama series on prevention, the NKFS disseminates the importance of healthy lifestyle, health screening, and prevention of CKD and kidney failure.

Details of the screening program are described elsewhere (26). Briefly, screening for urinary abnormalities and other risk factors for chronic diseases that could lead to CKD is targeted to four discrete populations, as follows: the working population through worksite screening; the general adult population through community-based screening; the pediatric population through school screening; and a specific occupational group, the taxi driver population of Singapore. Common features of the screening activities targeted to each of these populations are that screening is voluntary and is organized to facilitate the logistical needs of each group. In particular, the screening event is situated at locations convenient to each population, thereby facilitating their participation. In addition, all health screenings included the following examinations: (1) height and
weight measurements; (2) a clean-catch, midstream, random urine specimen, which was subjected to dipstick urinalysis; and (3) a minimum of two BP measurements accordingly to previously reported Joint National Committee VI guidelines (27). Additional tests performed on the three adult populations included random blood sugar and random cholesterol measurements. Data collection and health survey forms were also tailored to each of the populations. In addition, a validated nutritional survey for the Singapore population was also administered to the occupational screening cohort.

Individuals identified to have any screening abnormality receive onsite counseling by trained health screening nurses. These individuals are also advised to seek secondary screening and further treatment from their local physicians. Follow-up calls are then performed to ensure compliance with the recommendations provided by the nurse counselors.

A total of 621,183 Singaporeans have participated in the program from its inception in November 1997 to December 2001, of which 513,189, 91,793, 6757, and 9444 belonged to the worksite, community-based, occupational, and pediatric cohorts, respectively. It is beyond the scope of this manuscript to describe the results of this screening program, which have been presented previously (26). An analysis of the initial 189,177 who took part in the worksite screening program was performed to identify risk factors for proteinuria. The mean age of the participants was 36.3 ± 11.3 yr, and 53.1% were male; 77%, 10.5%, 8.9%, and 3.4% represented Chinese, Malay, Asian-Indian, and other racial groups, respectively. Current or prior exposure to smoking was observed in 18.0%. Body mass index values between 18.01 and 22.99 kg/m² were observed in 45.5% of subjects. Systolic BP (SBP) was ≥140 mmHg in 14.6% in this relatively healthy working population. Important predictors for proteinuria that have been identified in this uniquely Asian population include mild elevations in SBP and DBP, both extremes of body mass index, increasing age, and family history of renal disease (26). In addition, racial differences in prevalence of proteinuria were noted. Gender and current or prior smoking history were not independent predictors of proteinuria. These results suggest differences in risk factors for renal damage among Asians compared with Caucasians, which are of relevance in the design of more focused screening strategies as well as secondary and tertiary prevention programs.

Surveillance Program Identifies National Health Care Needs. One of the goals of the screening program is the identification of modifiable risk factors for CKD development. The epidemiology of ESRD in Singapore demonstrates that over 50% of incident ESRD is attributed to diabetes and hypertension (28), suggesting suboptimal control of these diseases thereby leading to complications that include kidney failure. Thus, data from the screening program were analyzed to determine the level of BP among patients with known hypertension or diabetes.

Of the 285,126 participants in the screening program from January 2000 to December 2001, known hypertension and diabetes mellitus were present in 7.9 and 2.5% of the population, respectively (29). Among those with pre-existing hypertension, 66.0% were found to have poorly controlled SBP, DBP or both. Furthermore, among patients with known diabetes mellitus, 64% had SBP levels >130 mmHg and 42.8% had DBP >80 mmHg. Thus, for these patients with either diabetes mellitus or hypertension, the level of BP control was suboptimal, placing the majority of these patients at increased risk for the development of CKD. Indeed, subgroup analysis of those with pre-existing hypertension or diabetes demonstrated that 5.7% and 7.9% had significant dipstick positive macroalbuminuria (≥1+ on dipstick) that was previously undetected. The poor control of BP in these populations at increased risk for CKD and the high prevalence rates of newly detected proteinuria in these populations support the value of the NKFS population-based screening program.

Early Intervention and Disease Management

Introduction. Because of the high incidence of ESRD attributed to diabetes and hypertension in Singapore (28); the poor BP control of these patients as evidenced by the NKFS screening program, and further corroborated by the Ministry of Health’s Survey (30); the poor glycemic control among patients with diabetes mellitus (30); and the observation that the majority of patients with diseases that lead to ESRD have access to varying standards of care, the early intervention and disease management program of the NKFS focuses on the improved management of patients with diabetes and hypertension. This component has the primary purpose of elevating the standards of care among the patients at increased risk of CKD, particularly among the population identified by the NKFS Screening Program. Given that effective intervention and renoprotection strategies exists for both diabetic and nondiabetic kidney disease, including the use of ACE inhibitors and angiotensin receptor blockers, antihypertensive therapy, and possibly the treatment of hyperlipidemia (18,31), the optimization of achieved care by patients at risk for kidney disease can be predicted to effect kidney disease prevention. Indeed, if cost-effectiveness were considered as a relevant criterion for the approach to kidney disease prevention, then nephropathy prevention, particularly diabetic nephropathy, has demonstrated to be the most cost-effective for type 2 diabetes and even cost-savings for type 1 diabetes (32). In this analysis, screening for diabetic nephropathy and subsequent treatment with ACE inhibitors were associated with a cost of $7,935 to $16,494 per patient per year, depending on assumptions regarding the effectiveness of ACEI in delaying CKD. Furthermore, improved glycemic control was similarly demonstrated to be a cost-effective strategy for preventing microvascular complications.

To evaluate the need for community-based comprehensive clinical services for patients with diabetes mellitus, 152 known diabetic subjects receiving outpatient care at private medical clinics, diagnosed for at least 1 yr and without previously detected nephropathy, were randomly evaluated for degree of diabetes control and the presence of other complications (Ramirez SPB, Maw P, Hsu SIH: A cross-sectional study of diabetes control and its associated complications in Singapore, manuscript in preparation). Poor glycemic control as defined by a hemoglobin A1c of ≥7.0% was observed in 73.7% of
these subjects and poor BP control as defined by a BP \(\geq 130/80\) mmHg was observed in 88.2%. Furthermore, 47.0% of subjects were found to have incipient diabetic nephropathy (presence of microalbuminuria defined by a urine albumin to creatinine ratio of 30 to 300 mg/g). These findings demonstrate the poor level of achieved care of these patients at increased risk of CKD.

With these in mind, the NKFS Prevention Program developed its secondary prevention strategy with a focus on diabetes mellitus and hypertension. This program, which is being implemented, involves two inter-related components: (1) the development of a disease management program in partnership with the primary care physician community; and (2) the provision of team-based comprehensive clinical care services, demonstrated to be critical in the proper management of complex chronic diseases like diabetes and hypertension (33).

Materials and Methods. In planning the secondary prevention program for Singapore, the country’s health care delivery system was taken into consideration. Outpatient medical care is generally provided by primary care physicians who are largely limited in their ability to administer comprehensive treatment of patients at risk for CKD. For instance, these private clinics are not equipped to detect microalbuminuria in the case of diabetic nephropathy. Furthermore, such outpatient care is generally paid for out-of-pocket (34) thereby resulting in the lack of a systematic method for tracking physician practice patterns, as well as the monitoring of clinical outcomes of patients. As such, programs that focus on preventing the development of kidney disease in patients with diabetes and hypertension need to be developed in close partnership with the general medical community of the country.

The NKFS initiated a formal partnership with the country’s general practitioner community in 2001. Representative physicians were invited to participate in an NKFS-initiated training program designed to achieve optimal standards of care for diabetic patients at risk for CKD. This training session was developed in collaboration with a disease management provider, the International Diabetes Center, a World Health Organization designated expert center in diabetes disease management. This program, which has been demonstrated to significantly improve both short- and long-term clinical outcomes in various populations (35,36), was modified through a customization session that included the participation of 10% of the country’s entire primary care physician population. Similar disease management programs have been demonstrated to result in significant improvements in both clinical and economic outcomes for patients with complex chronic diseases (37). Supplementing this disease management program is a continuing medical education program and an electronic medical records system that facilitates the implementation of the clinical care algorithms.

Equally important to educating the medical community regarding approaches to the prevention of CKD is the provision of comprehensive facilities and services that can facilitate the optimization of patient care. The NKFS is building a network of prevention centers staffed only by trained nurse specialists, who with primary care physicians will co-manage high-risk patients to lower their overall risk for complications of diabetes and hypertension, not limited to CKD. These services include general patient and family education, specialized screening for complications, individual education to provide patients with the skills for self-management, all of which will follow algorithms of care based on the disease management system described previously. Each patient will be assigned a nurse case manager who will ensure continuity of medical care and progress in achieving treatment goals. These Prevention Centers will also be supported by an electronic medical records system that will facilitate communications with the medical community, while enhancing the monitoring of the patient’s short- and long-term clinical outcomes. Although the current focus of these Prevention Centers is the elevation in the standards of care of patients with diabetes mellitus and hypertension to prevent or delay the development or progression of their renal complications, this framework will also be used to facilitate improvement in the care of any etiology of CKD, including glomerulonephritis.

Discussion

The NKFS Prevention Program incorporates a public health approach to the prevention of CKD. Its multiple strategies have been developed around the framework of the natural history of progression of kidney disease and its predisposing factors. Components of the program include surveillance for kidney disease and associated chronic diseases, a disease management program designed to improve physician practice patterns, and the provision of comprehensive services in the community through a network of Prevention Centers to optimize the care of patients at risk for kidney disease. Several components of this program are in the phase of active implementation such that clinical outcomes evaluating its efficacy are not yet available.

Given the multiracial make-up of the Singaporean population and the distinct logistical advantages of a “captured” population, the NKFS Prevention Program offers a unique opportunity for population-based studies on kidney disease. These include the determination of race-specific modifiable risk factors for kidney disease, the performance of longitudinal cohort studies evaluating the efficacy of renal disease screening, as well as a population for which race-specific risk prediction equations can be validated. Indeed, the NKFS nationwide prevention and screening initiative will provide benchmarks by which improvement in medical care can be measured, while continuing to provide future directions for further optimization of disease prevention paradigms.

References

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