J Med Sci 2015;35(2):50-56 DOI: 10.4103/1011-4564.156007 Copyright © 2015 JMS

ORIGINAL ARTICLE



Prevalence and Factors Associated with Chronic Kidney Disease among Military Aircrews

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Background: Recently, the number of patients diagnosed with end-stage renal disease (ESRD) in Taiwan has been rising. ESRD is known to typically develop from chronic kidney disease (CKD). The objectives of the study were to describe the prevalence of CKD and to evaluate the associated factors among military aircrews. Materials and Methods: In this study, military aircrews that received physical examinations in four military hospitals between 2004 and 2010 were selected. The abbreviated modification of diet in renal disease (aMDRD) formula was used to calculate glomerular filtration rates (GFRs). Urine protein, urine red blood cells, and urine pH values were used to define whether patients had CKD. This study analyzed 1317 cases. Results: The prevalence of CKD was 10.4% in the military aircrews. The risk of CKD was statistically significant higher in positive urine occult blood, high bilirubin, hyperuricemia, high total cholesterol, and each additional 1-year of age with odds ratio (95% confidence interval): 6.53 (3.86-11.06), 2.62 (1.28-5.37), 1.95 (1.11-3.42), 1.76 (1.05-2.95), and 1.03 (1.00-1.07), respectively. Conclusions: The majority of the participants diagnosed with CKD were in the early stages of the disease. The aMDRD formula could be calculated from annual physical examination results for using to understand GFRs and increase awareness of the kidney function, thereby delaying disease progression.

Key words: Prevalence, military, chronic kidney disease, physical examination

INTRODUCTION

Chronic kidney disease (CKD) has become one of the most prevalent diseases worldwide. The prevalence of kidney disease in each country varies between approximately 10% and 14%. For example, 1999-2004 National Health Nutrition Examinations Survey indicated that the prevalence of CKD in the United States was 13.07%. Taiwanese scholars analyzed 1999-2006 MJ health screening database and found that the prevalence of CKD in Taiwan was 11.93%, affecting approximately 2 million people. However, the awareness rate was only 3.5%. CKD does not have obvious symptoms. Approximately, 80-90% of patients with undiagnosed kidney

Received: October 6, 2014; Revised: November 10, 2014; Accepted: January 13, 2015

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disease are in the end-stages of the disease once symptoms begin to present. End-stage renal disease (ESRD) typically develops from CKD. Long-term data indicated that the number of ESRD patients in Taiwan increased by 64.95% between 1999 and 2008, and by 35.29% in the United States.³ This indicates that the number of ESRD patients in Taiwan grew rapidly over those 10 years.

Kidney disease (e.g., nephritis, nephrotic syndrome, and nephrosis) has consistently been one of the leading 10 causes of death in Taiwan over the past 10 years.⁴ Although kidney disease is not as severe as malignant tumors, heart disease, and cerebrovascular disease, deteriorating kidney function increases the risk of death, particularly that from cardiovascular disease.⁵ Once ESRD develops, kidney transplantation or lifelong hemodialysis is required to sustain life. ESRD is also frequently accompanied by complications such as cardiovascular disease.⁶ Because 99% population in Taiwan is covered by National Health Insurance (NHI) program, patients with uremia are not burdened by tremendous medical expenses for receiving hemodialysis to extend their lives.⁷ This may explain the high prevalence of ESRD among Taiwanese people. Data from the NHI administration indicated

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that 37 billion health insurance points were spent on outpatient and inpatient hemodialysis in 2008. The average point value for hemodialysis in that year was 0.92, which is approximately NT\$34 billion or 8.08% of total health care expenditures. This is the highest amount for any single disease in Taiwan and indicates that kidney disease treatment utilizes considerable national medical resources. Early prevention of kidney disease can slow the progression of CKD and reduce the occurrence of ESRD, lowering health insurance expenditures.

Military aircrews are considered to be professional, effective, and high-cost training for the military workforce to meet the increased-demands of national defense. Therefore, risk assessment of diseases is a major issue for military aircrews to prevent the suspected patients into CKD. The purpose of this study was thus to describe the prevalence of CKD and to evaluate the associated factors among military aircrews.

MATERIALS AND METHODS

Subjects

Participants were 1398 aircrew members who received at least one aircrew physical examination between 2004 and 2010 at any of the following military hospitals: Taoyuan Armed Forces General Hospital, Taichung Armed Forces General Hospital, Kaohsiung Armed Forces General Hospital, and Hualien Armed Forces General Hospital. The participant data were exported from each hospital information system. Medical record numbers were linked with identification numbers, birthdates, and physical examination data. After linking, the full names and identification numbers were delinked using serial numbers as substitutes to protect personal privacy. The participants were screened by using the most recent examination data of each person and removing those whose medical data were incomplete (including age and serum creatinine level), for an effective sample of 1317 people. This study was exempted from full review and their written informed consents of participants, and approved by the Tri-Service General Hospital Institutional Review Board (TSGHIRB, approval number 098-05-237) because the participants remained anonymous and the identification of participants had already encrypted, thereby complying with the Declaration of Helsinki without violation of participant privacy.

A blood sample was collected into an EDTA anticoagulant tube for each participant in this study. Standard enzymatic methods and electrophoresis were used to determine serum levels of lipids, including total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides. Fasting plasma glucose

level was measured by the hexokinase glucose-6-phosphate dehydrogenase procedure. Serum uric acid level was assayed using the colorimetric uricase-peroxidase principle. All biochemical tests were performed using automatic analyzers (TBA-200FR, Toshiba Corporation, Tokyo, Japan).

Definition of chronic kidney disease

This study was a cross-sectional study and used the abbreviated modification of diet in renal disease (aMDRD) formula suggested by the Taiwan Society of Nephrology to estimate glomerular filtration rates (GFR). The formula is as follows: Estimated GFR (eGFR) = 186.3 × serum creatinine $^{-1.154}$ × age $^{-0.203}$ × 0.742 (if female). The formula is consistent with the criteria for defining CKD from the kidney disease outcomes quality initiative of the U.S. National Kidney Foundation.¹⁰ Accordingly, a CKD event was defined as a reduced eGFR (<60 mL/min/1.73 m²), indicating stage 3 CKD according to the National Kidney Foundation staging system used in the Chinese population in Taiwan.² Those exhibiting GFRs in the range of the first and second CKD stages were required to also possess one of the following test results: Positive for urine protein, positive for red blood cells in urine, or a urine pH value >8.

Statistical analysis

The IBM SPSS statistics version 22 (IBM® SPSS® statistics 22) was used for data entry and statistical analysis. Demographic characteristics were described by means, standard deviations and percentages. Group differences were determined by independent t-tests and Chi-square test or Fisher's exact test. Multiple logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between the potential risk factor levels and CKD risk. All statistical tests were two-tailed, and values of P < 0.05 were considered statistically significant.

RESULTS

Table 1 shows the mean age of the participants was 36.43 ± 8.01 years. The majority were male (1292; 98.1%). Aircrafts were divided into fighter units (730 participants, 55.4%) and propeller units (587 participants, 44.6%). Hyperuricemia was present in 325 participants (a prevalence of 24.7%) and CKD was present in 137 participants (a prevalence of 10.4%). Average height was 172.94 ± 5.57 cm, average weight was 75.01 ± 9.88 kg, average body mass index (BMI) was 25.05 ± 2.82 kg/m², and average waist circumference was 83.26 ± 7.40 cm. The obesity criteria were a BMI of at least 30 kg/m². The results indicated that 705 (94.9%) participants had normal

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Table 1: Demographic data of military aircrews (n = 1317)

Variable	Number of participants (%)§	Average
Age		
20-29	352 (26.7)	36.43±8.01
30-39	500 (38.0)	
More than 40	465 (35.3)	
Sex		
Male	1292 (98.1)	
Female	25 (1.9)	
Aircraft type		
Fighter*	730 (55.4)	
Propeller [†]	587 (44.6)	
Hyperuricemia		
No	992 (75.3)	
Yes	325 (24.7)	
CKD‡		
No	1180 (89.6)	
Yes	137 (10.4)	
Stage 1	85 (6.5)	
Stage 2	49 (3.7)	
Stage 3	3 (0.2)	
Height (cm)	744	172.94±5.57
Weight (kg)	744	75.01±9.88
BMI (kg/m²)	744	25.05±2.82
Waist circumference (cm)	328	83.26±7.40
Body type#		
Normal	705 (94.9)	
Obese	38 (5.1)	
Systolic BP (mmHg)	736	123.74±10.06
Diastolic BP (mmHg)	736	75.28±9.27
BP**		
Normal	682 (92.8)	
Hypertensive	53 (7.2)	L C 120

*Fighters = F16, Mirage 2000, F-CK-1, and F5E/F; †Propellers = C-130, E2K, T-34, AT-3, and related departments and units; †GFR was calculated using the aMDRD formula. CKD was established for those meeting the criteria of NKF-KDOQI (2002). \$When the number of participants for each variable does not equal the total, this indicates missing values. The percentages are valid percentages. *Obesity diagnosis: BMI of at least 30. **Abnormal BP diagnosis: Systolic BP of at least 140 mmHg or diastolic BP of at least 90 mmHg. BMI = Body mass index; BP = Blood pressure; CKD = Chronic kidney disease; aMDRD = Abbreviated modification of diet in renal disease; GFR = Glomerular filtration rate

weight and 38 (5.1%) participants were obese. The average systolic blood pressure (BP) was 123.74 ± 10.06 mmHg and the average diastolic BP was 75.28 ± 9.27 mmHg. The criteria for hypertension were a systolic BP of at least 140 mmHg and a diastolic BP of at least 90 mmHg. The results indicated that

682 (92.8%) participants had normal BP and 53 (7.2%) had high BP.

In this sample [Table 2], 1180 of the aircrew members did not have CKD and their average age was 36.30 ± 8.11 . The 30-39 age group was a plurality of this number, comprising 444 (37.6%) crewmembers. CKD was exhibited by 137 crewmembers and their average age was 37.66 ± 7.06 . The >40 age group was a plurality of this number, comprising 57 (41.6%) crewmembers. The average age values demonstrated significant statistical differences between crewmembers with CKD and those without. The linear relationship between CKD stage and age was also statistically significant. In addition, the age group distribution of those with CKD and those without showed statistical significant differences.

The urinalysis data indicated that 128 (12.4%) of the aircrew members without CKD exhibited urine occult blood abnormalities. Urobilinogen test abnormalities were observed in 274 (33.5%) of these crewmembers. Among the aircrew members with CKD, 54 (45.4%) exhibited abnormal occult blood in the urine. Urobilinogen test abnormalities were observed in 40 (61.5%) of these crewmembers. The urinalysis data indicated that the distribution of urine occult blood and urobilinogen differed significantly between the crewmembers diagnosed with CKD and those without.

The biochemical blood test data indicated that the average values for total cholesterol, HDL, and total bilirubin were significantly different between the crewmembers with CKD and those without. The linear relationship between CKD stage, blood urea nitrogen (BUN), and serum creatinine was also statistically significant. In addition, the distribution of high total cholesterol and high total bilirubin differed significantly between the crewmembers with CKD and those without.

The univariate analysis results [Table 3] indicated that factors associated with CKD in the aircrew members were abnormal occult blood in the urine, abnormal urobilinogen, high total cholesterol, HDL, LDL, and high total bilirubin. After using logistic regression to control for age and sex, those exhibiting abnormal urine occult blood were at 5.91 times (95% CI: 3.93-8.88) greater risk of CKD than those without. Those exhibiting abnormal urobilinogen were at 3.56 times (95% CI: 2.06-6.15) greater risk of CKD than those without. Those demonstrating high total cholesterol were at 1.50 times (95% CI: 1.04-2.16) greater risk of early CKD than those without. Those presenting high total bilirubin were at 2.09 times (95% CI: 1.20-3.62) greater risk of CKD than those without.

The multivariate analysis results [Table 4] indicated that, after using logistic regression to control for other variables, participants exhibiting abnormal occult blood in the urine were at 6.53 times (95% CI: 3.86-11.06) greater risk of CKD

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Table 2: The distribution of age and biochemistry values between non-CKD and CKD in military aircrews

Variable -	Non-CKD ($n = 1180$)		CKD ($n = 137$)		t or χ^2 P^{\dagger}	P^{\dagger}		CKD stages		
	n (%)*	Average	n (%)*	Average			Stage 1	Stage 2	Stage 3	P^{\ddagger}
Age	1180	36.3088.11	137	37.66±7.06	2.113	0.036	36.58±7.48	39.29±6.03	42.00±4.58	0.016
20-29	328 (27.8)		24 (17.5)		6.911	0.032				
30-39	444 (37.6)		56 (40.9)							
More than 40	408 (34.6)		57 (41.6)							
Occult blood in urine										
Normal	908 (87.6)		65 (54.6)		85.217	< 0.001				
Abnormal	128 (12.4)		54 (45.4)							
Urobilinogen										
Normal	544 (66.5)		25 (38.5)		19.458	< 0.001				
Abnormal	274 (33.5)		40 (61.5)							
Fasting blood glucose	1169	95.58±12.51	130	93.35±10.17	1.962	0.050	92.05±10.81	95.79±8.83	89.50±5.71	0.140
Normal	817 (69.9)		97 (74.6)		1.037	0.309				
High blood glucose	352 (30.1)		33 (25.4)							
BUN	1180	14.05±3.06	137	14.52±3.34	1.696	0.090	13.98±3.28	15.25±3.31	17.97±0.83	0.007
Normal	1141 (96.7)		133 (97.1)			1.000				
Abnormal	39 (3.3)		4 (2.9)							
Uric acid	1180	6.23±1.17	137	6.34±1.14	1.057	0.291	6.28±1.19	6.39±1.01	7.17±1.91	0.287
Normal	894 (75.8)		98 (71.5)		0.965	0.326				
Abnormal	286 (24.2)		39 (28.5)							
Serum creatinine	1180	0.96±0.14	137	0.96±0.15	0.256	0.798	0.88 ± 0.10	1.07±0.08	1.43±0.06	< 0.001
Normal	1086 (92.0)		130 (94.9)		1.040	0.308				
Abnormal	94 (8.0)		7 (5.1)							
Total cholesterol	1180	189.60±32.44	137	198.62±43.81	2.337	0.021	198.68±45.81	199.12±41.78	188.73±18.51	0.899
Normal	781 (66.2)		76 (55.5)		5.735	0.017				
High	399 (33.8)		61 (44.5)							
HDL	1174	52.75±13.81	137	56.68±16.31	2.711	0.007	58.40±17.45	53.85±14.33	54.17±6.03	0.132
Normal	980 (83.5)		123 (89.8)		3.197	0.074				
Low	194 (16.5)		14 (10.2)							
Total bilirubin	838	0.75±0.33	105	0.84±0.36	2.468	0.014	0.84 ± 0.40	0.82±0.27	0.99±0.54	0.813
Normal	759 (90.6)		86 (81.9)		6.626	0.010				
High	79 (9.4)		19 (18.1)							

*When the number of participants for each variable does not equal the total, this indicates missing values. The percentages are valid percentages. †The *P* value for continuous variables is the two-tailed significance level of the independent samples *t*-test. The *P* value for categorical variables is the two-tailed significance level of the Chi-square test (or Fisher's exact test if any of expected cell count<5). ‡Here, the *P* value is the trend test. HDL = High-density lipoprotein; BUN = Blood urea nitrogen; CKD = Chronic kidney disease

than those without. Those exhibiting abnormal total bilirubin were at 2.62 times (95% CI: 1.28-5.37) greater risk of CKD than those without. Those exhibiting hyperuricemia were at 1.95 times (95% CI: 1.11-3.42) greater risk of CKD than those without. Those demonstrating high total cholesterol were at 1.76 times (95% CI: 1.05-2.95) greater risk of CKD than those without. Each additional 1-year of age increased the risk of CKD 1.03 times (95% CI: 1.00-1.07).

DISCUSSION

End-stage renal disease typically develops from CKD. The prevalence of CKD in Taiwan is estimated at 11.93% (stages 1-5 at the following respective percentages: 1.02%, 3.79%, 6.81%, 0.22%, and 0.10%) using the aMDRD formula based on 462,293 cases in the MJ health screening center database.² The aMDRD formula was also used in this study to obtain an

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Table 3: The crude and adjusted ORs and 95% CI for CKD in military aircrews

Variable	OR (95% CI)	Adjusted OR (95% CI)*
Age (years)	1.02 (1.00-1.04)	
Sex		
Male	1.00 (reference)	
Female	2.20 (0.81-5.95)	
Serum creatinine		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	0.62 (0.28-1.37)	0.64 (0.29-1.41)
Fasting blood glucose		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	0.79 (0.52-1.20)	0.72 (0.47-1.10)
Uric acid		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	1.24 (0.84-1.85)	1.27 (0.85-1.88)
BUN		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	0.88 (0.31-2.50)	0.87 (0.31-2.48)
Occult blood in urine		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	5.89 (3.93-8.84)§	5.91 (3.93-8.88)§
Urobilinogen		
Normal	1.00 (reference)	1.00 (reference)
Abnormal	3.18 (1.89-5.35)§	3.56 (2.06-6.15)§
Total cholesterol		
Normal	1.00 (reference)	1.00 (reference)
High	1.57 (1.10-2.25) [†]	1.50 (1.04-2.16) [†]
HDL		
Normal	1.00 (reference)	1.00 (reference)
Low	0.58 (0.32-1.02)	0.55 (0.31-0.99)†
Total Bilirubin		
Normal	1.00 (reference)	1.00 (reference)
High	2.12 (1.23-3.67)‡	2.09 (1.20-3.62)‡

^{*}Adjustment for age and sex. $^{\dagger}P < 0.05$; $^{\ddagger}P < 0.01$; $^{\$}P < 0.001$. HDL = High-density lipoprotein; BUN = Blood urea nitrogen; CKD = Chronic kidney disease; CI = Confidence interval; OR = Odds ratio

estimation. The results indicated a CKD prevalence of 10.4%, representing only stages 1-3 (at 6.45%, 3.72%, and 0.23%, respectively). Although this study found a lower prevalence of CKD in the earlier stages, this may be because the average age of participants in this study was low (36.4 vs. 41.8) or because of the effectiveness of the annual follow-up examinations that aircrew receive and early intervention provided by primary care teams. Increased age is a known risk factor of CKD, and the results of this study also indicated that the prevalence of CKD

Table 4: The multiple logistic regression of CKD in military aircrews

Variable	OR	95% CI	P
Age (per year)	1.03	1.00-1.07	0.044
High creatinine (vs. normal)	0.94	0.30-2.90	0.913
Hyperuricemia (vs. normal)	1.95	1.11-3.42	0.019
High BUN (vs. normal)	1.41	0.37-5.41	0.616
High blood glucose (vs. normal)	0.54	0.26-1.12	0.096
Occult blood in urine (vs. normal)	6.53	3.86-11.06	< 0.001
High total cholesterol (vs. normal)	1.76	1.05-2.95	0.033
Low HDL (vs. normal)	0.58	0.25-1.36	0.208
High total bilirubin (vs. normal)	2.62	1.28-5.37	0.009

CI = Confidence interval; OR = Odds ratio; HDL = High-density lipoprotein; BUN = Blood urea nitrogen; CKD = Chronic kidney disease

increased with age. However, a clear transition is observed at 45 years of age potentially because of the healthy worker effect. In addition, compared to studies on Taiwanese citizens from large-scale health screening organizations,² this study found a higher prevalence of CKD among participants older than 35 years. Therefore, increased kidney disease screenings for aircrew members older than 35 years are recommended.

An earlier study examined >5000 participants between the ages of 18 and 30 and conducted long-term follow-up for 13 years to understand the relationship between stress and BP. Ultimately, physiological measurements of >4000 participants who had completed three stress tests (i.e., cold pressor, star tracing, and video game tasks) were collected.11 The results indicated that substantial changes in BP after performing stress tests were associated with early onset of hypertension. In addition, young people who frequently experienced stress had a high likelihood of being diagnosed with hypertension early, at 40 years of age. Hypertension can lead to glomerular hypertension, hastened glomerular damage, inflammation, and decreased numbers of glomeruli.12 This ultimately affects kidney structure or function, causing CKD. The results of this study indicated that average values of systolic and diastolic BP and hypertension rates among aircrew in fighter aircrafts were higher than that of those in propeller aircrafts (7.7% vs. 6.6%). This may be because high-performance fighter aircrafts can accelerate to >6 G speeds instantaneously. Because of physiological limits, high-speed turns, diving, climbing, and other aircraft movements frequently lead to G-induced loss of consciousness in pilots.¹³ Thus, aircrew in fighter aircrafts sustain greater psychological stress than that of aircrew in propeller aircrafts. On the other hand, another explanation for the higher systolic BP provides a resistant affect in G-maneuvers with better sustainment in rapid acceleration.

This study used multivariate logistic regression analysis to predict the risk of CKD. The results indicated that occult

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blood in the urine, high total bilirubin, hyperuricemia, high total cholesterol, and each additional 1-year of age increased the risk of CKD. In each of these cases, the OR was increased 6.53 times (95% CI: 3.86-11.06), 2.62 times (95% CI: 1.28-5.37), 1.95 times (95% CI: 1.11-3.42), 1.76 times (95% CI: 1.05-2.95), and 1.03 times (95% CI: 1.00-1.07), respectively. Relevant studies have speculated that hyperuricemia may lead to glomerular hypertension. 14 Increases in BUN indicate a deteriorated capability of removing metabolized protein from the kidneys. Increases in blood glucose can lead to vascular injury through insulin resistance and abnormal regulation of vascular nitric oxide. 15 Clinically, occult blood in the urine typically appears in patients with IgA nephritis (glomerular lesions derived from the deposition of serum IgA antibodies in the glomerular basement membrane; this is a common form of nephropathy). In addition to being a common complication of CKD, studies have indicated that anemia is an independent predictor of kidney disease.12 This may be because anemia causes increases in renal plasma flow and excessive glomerular filtration, thereby leading to the development of proteinuria, hypertension, and ESRD.¹⁶ Dyslipidemia can also accelerate inflammation response, thereby resulting in reduced glomerular function.¹² Therefore, in addition to the factors used typically to predict CKD, such as proteinuria, increased age, and male sex, other nonconventional factors, such as uric acid, anemia, and occult blood in the urine, can also be employed to predict CKD incidence.

There were several limitations in this study. The military hospitals selected in this study were those that were capable of coordinating with the study schedule. Thus, they were selected by using purposive sampling. The marital status, medical history, and health behaviors of the participants could not be obtained. Therefore, the association between these factors and CKD was not investigated. The aMDRD formula is geared toward predicting CKD stages 3-5; however, there would be a potential bias for the personnel in our study who actually have CKD 1 or 2, as a false positive of our findings for predicting the population in the early stages of CKD. This study was a cross-sectional study, and only the association between CKD and demographic characteristics, physiological indicators, and biochemical blood tests could be examined. Consequently, the results cannot be interpreted as showing causality. In addition, because of the specialized work of the participants, the healthy worker effect was likely to occur. Thus, cases with CKD in stages 3-5 were not present, and inferences based on this study must be relatively conservative. The physical examination data from different years at each hospital were frequently incomplete. Therefore, the data presented a number of missing values, and complete data from all cases could not

be analyzed during multivariate analysis. This might have led to a lack of statistical significance among the variables, restricting the inferences derived from the results. There was an inverse association between fasting blood glucose and CKD in this study. Although fasting blood glucose seems higher in non-CKD participants than in CKD participants (95.58 mg/dL vs. 93.35 mg/dL), the levels of fasting blood glucose are both under the criteria of high blood glucose with ≤100 mg/dL. In addition, when we stratified the level of blood glucose followed the criteria of high blood glucose, there is no statistically significant association between fasting blood glucose in this study.

This study found that the prevalence of CKD among 1317 aircrew members at an average age of 36.4, 98.1% of whom were male, was 10.4%. The risk of CKD was 6.53 times, 2.62 times, 1.95 times, 1.76 times, and 1.03 times greater with positive urine occult blood results, high bilirubin, hyperuricemia, high total cholesterol, and each additional 1-year of age, respectively. The majority of the participants diagnosed with CKD were in the early stages of the disease. The aMDRD formula could be calculated from annual physical examination results for using to understand GFRs and increase awareness of the kidney function, thereby delaying disease progression. Therefore, once the military aircrews are suffered by the risk factors described above, the military health department is suggest to have further health managements for the high risk group of CKD.

ACKNOWLEDGMENTS

We thank the grant from Ministry of National Defense, Taiwan, Republic of China. Grant number D99-I07.

DISCLOSURE

No conflict of interest has been declared by the authors.

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