Prevalence of Chronic Kidney Disease in Thai Adult Population

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Objective: *Chronic kidney disease (CKD) is a major public health problem worldwide. Until now, no large-scale data about the prevalence of pre-dialysis CKD has been reported in Thailand.*
Material and Method: *The clinical and laboratory data from the ground air force personnel who were routinely checked up during 2002-2003 were collected and descriptively analyzed. The pilots and air crews were excluded. All personnel were working in Bangkok.*
Results: *15,612 RTAF personnel completed the annual check up. Eighty-two percent were male. The average age was 45.7 8 (19 - 65) years. According to the classification of stages of CKD by Kidney Disease Outcome Quality Initiative (K/DOQI), the prevalence of CKD is 9.1% by Cockcroft Gault formula and 4.6% by Modification of Diet in Renal Disease.*

Patients with diabetes mellitus, hypertension, hypercholesterolemia and proteinuria were found in 8.2%, 45.8 %, 28.2 % and 1.8% respectively. CKD patients were older, had higher body weight, Body Mass Index (BMI), blood pressure and blood sugar than non CKD personnel.
Conclusion: *CKD were not uncommon among RTAF personnel. The Cockcroft-Gault and MDRD equations were different in detecting CKD in the present study. The appropriate equation to determine GFR in Thai population should be evaluated. Low sensitivity of dipstick proteinuria may cause the low prevalence of stage 1 and 2 CKD.*

Keywords: *Prevalence, Chronic kidney disease, Glomerular filtration rate, Creatinine clearance*

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Chronic kidney disease (CKD) is a major public health problem worldwide including Thailand. Patients suffering from CKD experience uremic and cardiovascular complications. They end up to be end stage renal disease (ESRD) patients who have to be dialyzed or have a kidney transplantation, an expensive treatments. Early detection and intervention of CKD can prevent or slow kidney disease progression and should reduce the burden of the disease[1,2]. However, many CKD patients are not detected and properly managed at an early stage[3-6]. The important factor causing delayed diagnosis is non-standardization of definition and classification of CKD in the past[7]. However, all data from the national registry around the world show rapidly increasing numbers of ESRD[8-12].

In 2002, the National Kidney Foundation (NKF) introduced a standard guideline for diagnosis, definition and classification of CKD that was published in the Kidney Disease Outcomes Quality Initiative (K/DOQI). The definition of CKD in this guideline is kidney damage for more than 3 months, as defined by structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR), or GFR less than 60 ml/min/1.73 m^2 for more than 3 months with or without kidney damage[13]. The K/DOQI also classifies CKD into five stages according to GFR.

The prevalence of CKD has been reported in many countries. In USA, the Third National Health and

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Nutrition Examination Survey (NHANES III) showed 11 percent (19.2 millions) were diagnosed as CKD. According to the K/DOQI classification, they found CKD stage 1 (persistent albuminuria with normal GFR) in 3.3%, stage 2 (persistent albuminuria with GFR 60-89 ml/min/1.73m^2) in 3.0%, stage 3 (GFR 30-59 ml/min/ 1.73m^2) in 4.3%, stage 4 (GFR 15-29 ml/min/1.73m^2) in 0.2% and stage 5 (GFR less than 15 ml/min/1.73m^2) in 0.2% of US population[14]. The prevalence of CKD in the western part of Australia was 16 percent[15]. In Singapore, a south-east Asian country, reported the CKD prevalence of 10.1 percent[16].

Information from a large-scale population about the prevalence of pre-dialysis CKD has been reported in Thailand. Only a publication from the Thailand Renal Replacement Therapy (TRT) registry including ESRD patients who require renal replacement was reported. In the year 2000, TRT registry showed that the prevalence of ESRD patients in Thailand was 1,995 cases[17]. The recent unpublished data from TRT showed the prevalence of ESRD at the end of 2004 was 13,597 cases. The purpose of the present study was to identify the prevalence in CKD in a Thai population.

Material and Method

A descriptive study was done in Department of Preventive Medicine, Directorate of Medical Services, Royal Thai Air Force (RTAF). The clinical and laboratory data from RTAF personnel who were routinely checked up from January 2002 to December 2003 were collected and descriptively analyzed. The pilots and air crews were excluded. All personnel were working in Bangkok. Only data from personnel that were completely checked were included in the present study. Routine history taking and physical examination were done in all the personnel. The laboratory analysis results including fasting plasma glucose, blood urea nitrogen, serum creatinine, serum total cholesterol, serum triglyceride, serum high density lipoprotein and urine for protein were analyzed.

The definition and classification of CKD in K/DOQI guideline 2002 was used in the present study[13]. Because urine albumin was not included in the routine check up, kidney damage in stage 1 and 2 in the present study was identified as positive urine protein more than 1+.

Blood pressure was measured in the sitting position using an automatic sphygmomanometer (KENZ model BPMSP-1). All people were rested for 5 minutes before blood pressure measurement. If the results of systolic or diastolic blood pressure were more than 140 or 90 mmHg respectively, blood pressure would be rechecked after a one-hour rest. Hypertension was defined according to the Seventh Joint National Committee for prevention and treatment of hypertension (JNC VII)[18]. The normal blood pressure is systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg. Hypertension was defined as systolic blood pressure more than 140 mmHg or diastolic blood pressure more than 90 mmHg or taking an antihypertensive medication.

Diabetes mellitus was diagnosed if a fasting plasma glucose more than 126 mg/dl or taking oral hypoglycemic agent or insulin. Urine protein was checked by using random spontaneously void fresh urine (mid stream) technique by uristrix and proteinuria was identified if the result shows positive more than 1+.

Blood samples for fasting plasma glucose, blood urea nitrogen, serum creatinine, total cholesterol, triglycerides and HDL cholesterol were taken after 12-hour fasting. All chemistries were analyzed using an automate analyzer (Hitachi 717 analyzer) and reported in conventional units. Serum creatinine were measured by modified kinetic Jaffe's reaction using the same automate analyzer.

Estimated GFR was calculated using the Modification of Diet in Renal Disease Study (MDRD) equation [GFR = 186.3 x (serum creatinine)$^{-1.154}$ x (age)$^{-0..203}$ x (0.742 for women)]. Creatinine clearance was estimated by the Cockcroft-Gault formula [Ccr = (140 - age) x body surface area (m^2) x body weight (kg) / (serum creatinine x 72 x 1.73 m^2) x (0.85 for women)]. Body surface area is calculated by an equation = 0.20247 x Height(m)$^{0.725}$ x Body weight(kg)$^{0.425}$. BMI was defined as body weight (kg) / Height (m)^2.

Statistical analysis

All data are expressed in number, mean $\pm$ Standard Deviation (SD). Statistical comparison was performed using independent t-test and comparison of percentage between groups was made with the Chi-square test. Correlation analysis between calculated creatinine clearance and calculated GFR was applied. Statistical analysis was performed using SPSS software version 12 for window. All probabilities were two-tailed and the level of significance was set at p value less than 0.05.

Results

Nineteen thousand,eight hundred and seventy-nine people were routinely checked during the year 2002 to 2003. Uncompleted and duplicated data were

shown in 4,267 records. The clinical and laboratory data of 15,612 cases were included in the present study.

Most of them were male (12,775 cases, 82%). Mean age was 45.7 ± 8 (range 19-65) years. The prevalence of diabetes mellitus was 8.2 percent. Hypertension was diagnosed in 46.4 percent. Hypercholesterolemia defined as total cholesterol more than 200 mg/dl was found in 28.2 percent.

Table 1. Epidemiologic data of the study population (N = 15612)

	Mean ± Standard deviation	minimum-maximum
Age (yr)	45.7 ± 8	19-65
Body weight (kg)	67.4 ± 11.7	35.9-134.4
Height (cm)	165.2 ± 7.1	122-198
Body mass index (kg/m^2)	24.67 ± 3.7	12-52
Systolic blood pressure (mmHg)	138 ± 21	72-249
Diastolic blood pressure (mmHg)	81.5 ± 14	41-157
Mean arterial pressure (mmHg)	100.4 ± 15.8	53-185
Fasting plasma glucose (mg/dl)	101 ± 32	40-620
Total cholesterol (mg/dl)	226.9 ± 46.7	34-696
Triglyceride (mg/dl)	164 ± 120	47-1598
HDL cholesterol (mg/dl)	51.6 ± 14.4	2-238
LDL cholesterol (mg/dl)	142.4 ± 44.5	167-462
Creatinine Clearance* (ml/min/m^2)	94.2 ± 30.8	4.78-720
GFR** (ml/min/m^2)	89.9 ± 22.4	4.19-570

* Creatinine clearance calculated by the Cockcroft-Gault formula

** Glomerular filtration rate calculated by the Modified Diet in Renal Disease (MDRD) Study equation

Table 2. Epidemiologic data of the study population (N = 15612)

		Number of subjects	%
Gender	Male	12,775	82
	Female	2,837	18
Age distribution (years)	15-19	8	0.05
Mean age 45.7 ± 8	20-24	173	1.1
	25-29	27	0.18
	30-34	593	3.9
	35-39	2,339	15.2
	40-44	3,692	24.0
	45-49	2,718	17.7
	50-54	3,694	24.0
	55-59	1,766	11.5
	60-65	354	2.3
Not specify		248	
Diabetes mellitus	Yes	1,273	8.2
	No	14,339	91.8
Body mass index (kg/m^2)	≤ 18	259	1.7
	18.01-22.99	4,984	32.5
	23.0-24.99	3,443	22.4
	25.0-27.49	3,571	23.3
	27.5-29.9	1,859	12.1
	≥ 30	1,220	8.0
Not specify		276	
Hypercholesterolemia	Yes	4,409	28.2
	No	11,203	71.8

About one-third of the population (4,984 cases, 32.5%) had a normal BMI (18.01-22.99 kg/m^2) and 1,220 cases (8.0%) had a BMI of more than or equal to 30 kg/m^2 and is classified as obesity. Characteristics of the study population are shown in Table 1 and 2.

The authors found dipstick proteinuria in 1.9 percent of the population. Most of them were 4+ proteinuria (0.8%). The people with proteinuria were significantly older, had a higher body weight, BMI, systolic blood pressure, diastolic blood pressure, mean arterial pressure, fasting plasma glucose, total cholesterol and triglyceride when compared to the people without proteinuria (Table 4). Hypertension was diagnosed in 46.1 percent (stage 1 in 28.0% and stage 2 in 18.1%). Number and percent of population according to blood pressure classification of JNC 7 is shown in Table 5.

Table 6 shows the CKD prevalence in the study population. When using Cockcroft-Gault formula to calculate creatinine clearance, the prevalence of CKD was 9.1%. Less CKD prevalence was found when calculate GFR by the MDRD equation (4.6%). Using GFR criteria for CKD (GFR < 60 ml/min/1.73m^2), the authors found stage 3 to 5 CKD in 7.5% when using the Cockcroft-Gault formula and 3.1% of the population when using MDRD equation. However, calculated creatinine clearance by the Cockcroft-Gault formula

Table 3. Prevalence of proteinuria in study population

Proteinuria	Number of subjects (N = 15612)	%
negative	15331	98.1
1+	6	0.4
2+	55	0.4
3+	4	0.3
4+	118	0.8

Table 5. Prevalence of hypertension classified as JNC 7 in study population (N = 15522)

Hypertension	Number of Subjects	%
Normal	2,705	17.4
Prehypertension	5,658	36.5
Hypertension		
stage 1	4,348	28.1
stage 2	2,811	18.0

Table 4. Comparison between the population with and without proteinuria

	With proteinuria	Without proteinuria	p-value
Age (yr)	48.5 ± 6.7	45.67 ± 8	<0.0001
Body weight (kg)	72.2 ± 13.1	67.3 ± 11.6	<0.0001
Body mass index (kg/m^2)	26.2 ± 4.8	24.6 ± 3.7	<0.0001
Systolic blood pressure (mmHg)	149.4 ± 26.8	138 ± 21	<0.0001
Diastolic blood pressure (mmHg)	88.4 ± 16.4	81.4 ± 14	<0.0001
Mean arterial pressure (mmHg)	108.7 ± 19.2	100.3 ± 15.7	<0.0001
Fasting plasma glucose (mg/dl)	163.5 ± 80	100.2 ± 29	<0.0001
Total cholesterol (mg/dl)	235.7 ± 48.2	226.7 ± 46.6	<0.0001
Triglycerides (mg/dl)	206 ± 146	163.4 ± 119	<0.0001
HDL cholesterol (mg/dl)	49 ± 12.9	51.6 ± 14.3	<0.0001
LDL cholesterol (mg/dl)	145.5 ± 45.5	142.4 ± 44.5	<0.0001

Table 6. Prevalence and staging of CKD in study population (N = 15,612)

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Total
	GFR > 90 ± Proteinuria	GFR 60-89 ± Proteinuria	GFR 30-59	GFR 15-29	GFR < 15	
CCr* (C-G)	150 (1.0%)	94 (0.6%)	1135 (7.3%)	18 (0.1%)	8 (0.05%)	1405 (9.1%)
GFR** (MDRD)	128 (0.8%)	112 (0.7%)	460 (2.9%)	14 (0.1%)	9 (0.06%)	723 (4.6%)

* Creatinine clearance calculated by the Cockcroft-Gault formula

** Glomerular filtration rate calculated by the Modified Diet in Renal Disease (MDRD) Study equation

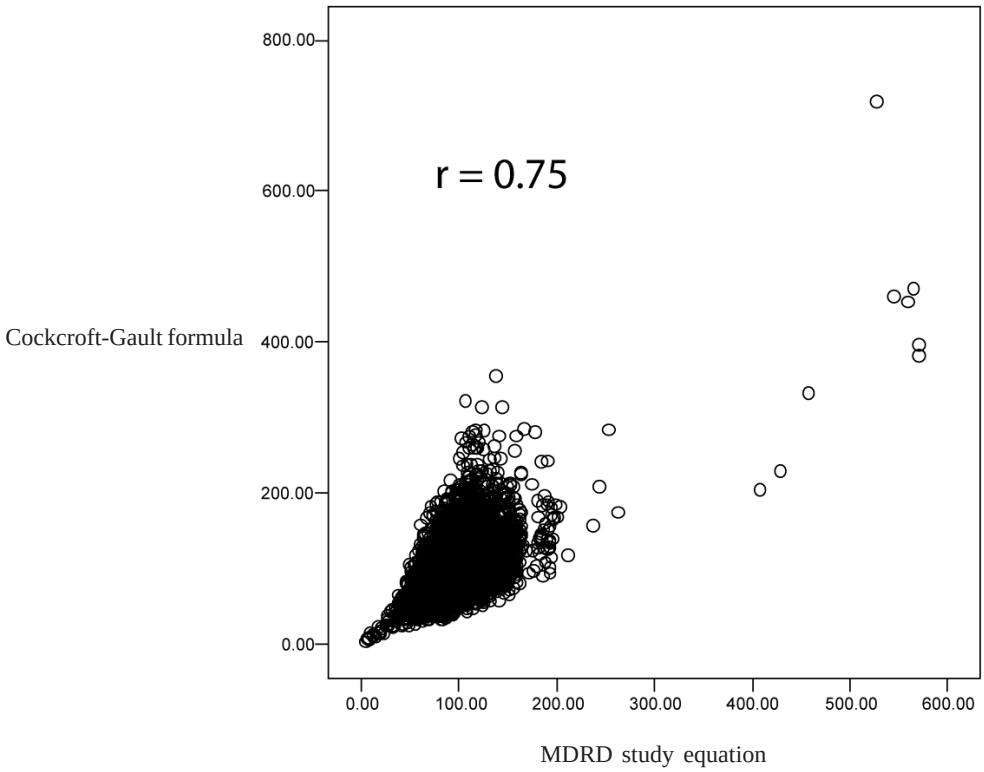

Fig. 1 Graph showed correlation between calculated creatinine clearance using Cockcroft-Gault formula (Y-axis) and calculated GFR using MDRD study equation (X-axis)

had statistical significant correlation with calculated GFR by the MDRD equation (r = 0.75). Fig. 1 shows this correlation. Most CKD patients were classified in stage 3.

The authors found a significantly higher body weight, BMI, fasting plasma glucose and triglyceride in the CKD group when compared with the non-CKD group either using the Cockcroft-Gault or MDRD formula (Table 7 and 8). HDL cholesterol level was lower in the CKD group. Only the CKD group that was diagnosed using the Cockcroft-Gault formula had significant higher systolic blood pressure, diastolic blood pressure and total cholesterol level when compared to non-CKD group. The authors did not find any difference in these factors when calculating GFR by the MDRD equation.

Table 7. Comparison between the population with and without CKD when calculate GFR using the MDRD equation

	CKD	non CKD	p-value
Age (yr)	49.5 ± 6.9	45.5 ± 8	<0.0001
Body weight (kg)	25.8 ± 3.8	24.6 ± 3.7	<0.0001
Body mass index (kg/m^2)	70.7 ± 11.8	67.3 ± 11.6	<0.0001
Systolic blood pressure (mmHg)	147.5 ± 25.1	137.9 ± 20.9	<0.0001
Diastolic blood pressure (mmHg)	86.5 ± 15.8	81.2 ± 14	<0.0001
Mean arterial pressure (mmHg)	106.8 ± 18.2	100.1 ± 15.6	<0.0001
Fasting plasma glucose (mg/dl)	130.8 ± 64.9	99.9 ± 28.7	<0.0001
Total cholesterol (mg/dl)	239.7 ± 54.4	226.3 ± 46.2	<0.0001
Triglycerides (mg/dl)	191.4 ± 130.4	162.8 ± 119.6	<0.0001
HDL cholesterol (mg/dl)	50.3 ± 14	51.6 ± 14.3	0.015
LDL cholesterol (mg/dl)	151.1 ± 50.2	142 ± 44.2	<0.0001

Table 8. Comparison between the population with and without CKD when calculate creatinine clearance using the Cockcroft-Gault formula

	CKD	non CKD	p-value
Age (yr)	50.4 ± 7.1	45.3 ± 7.9	<0.0001
Body weight (kg)	22.2 ± 3.7	24.9 ± 3.6	<0.0001
Body mass index (kg/m^2)	57.6 ± 11.5	68.5 ± 11.2	<0.0001
Systolic blood pressure (mmHg)	138.9 ± 24.3	138.2 ± 20.9	0.29
Diastolic blood pressure (mmHg)	81.3 ± 15.4	81.5 ± 14	0.62
Mean arterial pressure (mmHg)	100.5 ± 17.6	100.4 ± 15.6	0.82
Fasting plasma glucose (mg/dl)	111.9 ± 51.7	99.9 ± 29.2	<0.0001
Total cholesterol (mg/dl)	229.5 ± 48.3	226.6 ± 46.5	0.2
Triglycerides (mg/dl)	150 ± 109.9	165.6 ± 121.2	<0.0001
HDL cholesterol (mg/dl)	56 ± 15.8	51 ± 14	<0.0001
LDL cholesterol (mg/dl)	143.5 ±45.9	142.3 ± 44	0.342

Discussion

In the present study, the authors found the differences in age, fasting plasma glucose, blood pressure and lipid profile between population with and without CKD. Many epidemiological studies have reported the same factors correlated with CKD, ESRD and cardiovascular disease[19-21]. Control of blood sugar[22], blood pressure[23,24] and lipid[25] are shown to retard progression of CKD staging. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists[26-30] are also beneficial in CKD patients.

The prevalence of CKD was different between a model using creatinine calculated by the Cockcroft-Gault formula and GFR calculated by the MDRD Study equation. When using the Cockcroft-Gault formula, the CKD prevalence was 9.1%. When calculating GFR by MDRD equation, the CKD prevalence was less (4.6%). If the authors diagnosed CKD using GFR criteria (GFR < 60 ml/min/1.73m^2), The authors found stage 3 to 5 CKD in 7.5% and 3.1% of the population when using the Cockcroft-Gault or MDRD equation respectively. This prevalence of CKD by GFR criteria in the present study is very close to the previous report from the United States adult population: Third National Health and Nutrition Examination Survey (NHANE III)[14]. The US NHANE III showed that CKD stage 3 to 5 in the US adult population was 7%, if using the Cockcroft-Gault formula and 4.7%, if using the MDRD equation.

However, the numbers of population in the early stage of CKD (stage 1-2) in the present study were very low (1.8%). The data from the USA[14], Australia[15] and Singapore[16] have shown the prevalence of early CKD to be 6.3%, 7% and 10% respectively. The lower prevalence of early CKD in the present study was due to low sensitivity of dipstick proteinuria to detect the early CKD. Most of the reports from other countries used microalbuminuria and hematuria to detect kidney damage. This low sensitivity of routine dipstick proteinuria may cause a missed diagnosis of many patients with early CKD who may benefit from intervention to slow kidney progression,

In the present study the authors found the difference in the prevalence of CKD when using calculated creatinine clearance by the Cockcroft-Gault formula or calculated GFR by the MDRD equation especially in stage 3 (7.3% vs 2.9% respectively). The difference between the Cockcroft-Gault formula and the MDRD equation is due to the Cockcroft-Gault formula using age in calculation but not in the MDRD equation. Older populations will have low calculated creatinine clearance when using the Cockcroft-Gault formula. There are many publications concerning the difference between both calculations[31-37]. However, the results are conflicting about which one should be the gold standard for estimation of GFR. No study concerning this issue has been conducted in Thailand.

When extrapolating this prevalence of CKD in RTAF personnel to an age-matched Thai population, the authors found that the estimated prevalence of CKD stage 3 to 5 was 3,267,790 cases when using the Cockcroft-Gault formula and 1,350,686 cases when using the MDRD equation. Using the Cockcroft-Gault formula, estimated prevalence of CKD stage 3: 4: 5 were 3,180,649: 43,570: 43,570 respectively. Using the MDRD equation, estimated prevalence of CKD stage 3: 4: 5 were 1,263,545: 43,570: 43,570 respectively. The prevalence of stage 5 CKD who may require renal replacement therapy by this estimation out-numbered the Thailand Renal Replacement Therapy registry by five

times. This result may be explained by unequal performance of dialysis on the Thai population.

Conclusion

In conclusion, chronic kidney disease is not uncommon among the Thai adult population. The prevalence of CKD in RTAF personnel was 9.1% and 4.6% when using the Cockcroft-Gault formula and the Modification of Diet in Renal Disease Study (MDRD) equation respectively. The large difference in this prevalence is a major concern. However, no consensus has reported the best equation to calculate glomerular filtration rate in a Thai population. Further study concerning this issue should be done.

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ความชุกของโรคไตเรื้อรัง ในประชากรผู้ใหญ่ชาวไทย

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วัตถุประสงค์: *โรคไตเรื้อรัง (CDK) เป็นโรคที่เป็นปัญหาสาธารณสุขที่สำคัญของประเทศต่าง ๆ ทั่วโลก อย่างไรก็ตาม ยังไม่มีรายงานการศึกษาในประชากรจำนวนมากถึงความชุกของโรคไตเรื้อรังก่อนการล้างไตในประเทศไทย*

วัสดุและวิธีการ: *ผู้วิจัยได้รวบรวมข้อมูลประวัติและผลการตรวจทางห้องปฏิบัติการจากแฟ้มประวัติของบุคลากรกองทัพอากาศไทยที่มารับการตรวจร่างกายประจำปีที่กองเวชศาสตร์ป้องกัน กรมแพทย์ทหารอากาศในระหว่างปี พ.ศ. 2545 - พ.ศ. 2546 มาวิเคราะห์เพื่อศึกษาความชุกและปัจจัยที่มีความสัมพันธ์กับโรคไตเรื้อรัง โดยไม่ได้รวมข้อมูลของนักบินและผู้ทำงานในอากาศ บุคลากรที่รับการตรวจทั้งหมดทำงานในกรุงเทพมหานคร*

ผลการศึกษา: *บุคลากรกองทัพอากาศไทยจำนวน 15,612 คนได้รับการตรวจประจำปี เป็นผู้ชาย 86% มีอายุเฉลี่ยอยู่ในช่วง 45.7 $\pm$ 8 (19 - 65) ปี ความชุกของ CKD แต่ละระยะตาม Kidney Disease Outcome Quality Initiative (K/DOQI) เป็น 9.1% (Cockcroft Gault Formula) และ 4.6% (MDRD)*

พบเบาหวาน, ความดันโลหิตสูง, โคเลสเตอรอลในซีรั่มสูง และการมีโปรตีนในปัสสาวะ 8.2%, 45.8%, 28.2% และ 1.8% ตามลำดับ ผู้ป่วยที่เป็น CKD มีอายุ น้ำหนัก ค่าดัชนีมวลกาย ความดันโลหิต และระดับน้ำตาลในเลือดสูงกว่ากลุ่มที่ไม่เป็น CKD อย่างมีนัยสำคัญทางสถิติ

สรุป: *ภาวะ CKD พบได้ไม่น้อยในบุคลากรกองทัพอากาศไทย พบว่ามีความแตกต่างของความชุกของ CKD ที่ได้จากการคำนวณโดยสูตรของ Cockcroft-Gault และ MDRD ดังนั้นจึงจำเป็นต้องหาสูตรคำนวณที่เหมาะสมสำหรับคนไทยต่อไป การตรวจโปรตีนในปัสสาวะโดยใช้ dipstick มีความไวต่ำในการวินิจฉัย CKD ทำให้ความชุกของ CKD ระยะที่ 1 และ 2 ต่ำกว่าที่ควร*