ปัจจัยที่มีผลต่อโอกาสการเกิดภาวะไตเสื่อมของผู้ป่วยโรคเบาหวานชนิดที่ 2 โรงพยาบาลชุมชนบ้านนา จังหวัดนครนายก
Factors Affecting Kidney Failure in Patients with Type 2 Diabetes Mellitus in Banna Community Hospital, Nakhonnayok Province

นิพนธ์ต้นฉบับ

Original Article

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วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2563;15(1):37-42.

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Thai Pharmaceutical and Health Science Journal 2020;15(1):37-42.

บทคัดย่อ

วัตถุประสงค์: เพื่อวิเคราะห์ปัจจัยที่ส่งผลต่อโอกาสการเกิดภาวะไตเสื่อมในผู้ป่วยเบาหวานในโรงพยาบาลชุมชน **วิธีการศึกษา**: การศึกษาเชิงวิเคราะห์แบบย้อนหลัง ประชากรที่ศึกษาคือ ผู้ป่วยโรคเบาหวานในคลินิก รพ.บ้านนา จำนวน 3,250 คน สุ่มตัวอย่างแบบเป็นระบบ (Systematic random sampling) โดยเรียงลำดับตาม HN 1 คนเว้น 1 คน ได้คนไข้ 1,254 คน ใช้สถิติได้แก่ ค่าเฉลี่ยเลขคณิต ส่วนเบี่ยงเบนมาตรฐาน ค่าความถี่ ร้อยละ การวิเคราะห์ปัจจัยที่ส่งผลต่อโอกาสการเกิดภาวะไตเสื่อมของผู้ป่วยโรคเบาหวาน โดยใช้ค่า eGFR สะท้อนระดับภาวะไตเสื่อม ใช้การวิเคราะห์สมการถดถอยเชิงเส้น (stepwise linear regression) **ผลการศึกษา:** ปัจจัยที่มีผลต่อโอกาสระดับ eGFR ของผู้ป่วยโรคเบาหวานอย่างมีนัยสำคัญ (*P*-value < 0.05) ได้แก่ ค่าชีวเคมี ซึ่งค่าที่สัมพันธ์ทางลบ ได้แก่ creatinine ในเลือด (B = -44.28), HbA1C (B = -1.08) และ BUN (B = -0.49) และสัมพันธ์ทางบวกกับ HDL (B = 0.06) โดยทั้งหมดอธิบายความแปรปรวนของค่า eGFR ได้ร้อยละ 75 (R^2 = 0.75) ส่วนปัจจัยด้านพฤติกรรมสุขภาพมีเพียงพฤติกรรมการดื่มสุราหรือเครื่องดื่มที่มีแอลกอฮอลที่สัมพันธ์กับระดับ eGFR ทางลบอย่างมีนัยสำคัญทางสถิติ (B = -1.488) โดยอธิบายความแปรปรวนของระดับ eGFR ได้ร้อยละ 15 ทั้งนี้ ค่าดัชนีมวลรวมของร่างกาย (B = -0.407) และระยะเวลาเป็นเบาหวาน (B = -0.377) ที่สัมพันธ์กับ eGFR อย่างมีนัยสำคัญทางสถิติและสามารถทำนายความแปรปรวนของ eGFR ได้ร้อยละ 19 **สรุป:** ปัจจัยที่ส่งผลต่อโอกาสเกิดภาวะไตเสื่อมของผู้ป่วยเบาหวาน ได้แก่ creatinine HbA1C BUN HDL การดื่มสุราหรือเครื่องดื่มที่มีแอลกอฮอล์ ระยะเวลาที่เป็นเบาหวาน และดัชนีมวลรวมของร่างกาย

คำสำคัญ: เบาหวาน, ภาวะไตเสื่อม, ปัจจัยเสี่ยง

Abstract

Objective: To determine factors affecting the risk of kidney failure in diabetes patients in community hospital. **Method:** In this retrospective study, study population was 3,250 patients in diabetic clinic at Banna Hospital. A sample of 1,254 patients was selected using systematic random sampling with alternate HN. Descriptive statistics with mean with standard deviation and frequency with percentage were used. Stepwise linear regression analysis was used to examine factors affecting the eGFR as kidney failure indicator. **Results:** Factors significantly associated with eGFR (*P*-value < 0.05) were biochemistry factors with serum creatinine (B = -44.28), HbA1C (B = -1.08) and BUN (B = -0.49) of negative relation and HDL (B = 0.06) of positive relation. These factors could explain 75% of eGFR variance (R^2 = 0.75). For health behavior factors, only alcohol or alcoholic beverage intake was negatively associated with eGFR (B = -1.488) with 15% eGFR variance exaplained. In addition, body mass index (BMI) (B = -0.407) and duration of diabetes diagnosis (B = -0.377) were associated with eGFR with 19% variance explained. **Conclusion:** Factors affecting the decline of eGFR were serum creatinine, HbA1C, BUN, HDL, alcohol or alcoholic beverage intake, duration of diabetes diagnosis and BMI.

Keywords: diabetes, kidney failure, risk factors

Editorial note
Manuscript received in original form on September 11, 2019;
revised September 18, 2019;
and accepted in final form on December 19, 2019

Journal website: http://ejournals.swu.ac.th/index.php/pharm/index

Introduction

Type 2 diabetes mellitus has been an epidemic worldwide and Thailand was no exception. Based on the data from the Diabetes Association of Thailand, it has been predicted that there will be a total of 642 million cases of type 2 diabetes in 2045 worldwide.[1] As a critical public health problem of Thailand, the treatment of diabetes aims at lengthening the patient's lifespan and avoiding complications especially end-stage renal disease (ESRD). Chronic kidney disease (CKD) has been a global problem. In Thailand, and the study of Thai Medical Research Network (MedResNet) reported that prevalence of CKD in diabetes patients in 2009 was 17.5%.[2] At present, the annual expenditure for renal replacement therapy, both continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis was approximately 240,000 baht per patient. This expenditure has posed a high medical burden for the patient, their family and the public as a whole.

Based on the Thailand Renal Replacement Therapy Registry 2013 report[3], the major cause of ESRD undergoing renal replacement therapy was diabetes (37.5%). A total of 20 – 40% of type 2 diabetes were more likely to develop diabetic kidney disease.[4] The individuals were advanced to CKD and

eventually ESRD. With a higher prevalence of diabetes, a greater incidence of diabetes-related CKD was found.[5,6]

Based on the policy to reduce CKD incidence, the main indicators in the fiscal year of 2016 was at least 50% of the CKD patients could show down kidney impairment progression (a decline rate of eGFR of less than 4 ml/min/1.73 m^2). Based on the seven measures for management of CKD, it is indicated to prevent and slow down the progression of CKD in those with stage 1 – 3 CKD, and slow down the progression to ESRD in those with stage 4 – 5. In addition, it is recommended to promote the environment healthy to CKD patients, decrease risk factors, and promote CKD management in the community.[6] In the health administration region 4, only 62.80% of CKD patients could slow down the CKD progression which was in the 9th of all 12 regions.

As a hospital in the health administration region 4, Banna Community Hospital took care of a large number of diabetes patients. A number of diabetes patients at the out-patient department have increased from 2,768 to 2,950 and 3,250 cases in 2016, 2017 and 2018, respectively. A number of stage 3 – 5 CKD cases among diabetes patients have also been increasing every year.

The pression of CKD among diabetes patients resulted in a great financial burden and a high mortality risk. In Somdej Prapinklao Hospital, diabetes patients with renal complications had levels of BUN, serum creatinine, uric acid and urine albumin creatinine ratio significantly higher than those with no complications.[7] Factors predicting CKD in diabetes patients included uncontrolled glycemic status (as HbA1C), having co-morbidities, uncontrolled blood pressure, high-fat food intake, high diastolic blood pressure, high triglyceride, age of 70 – 79 years, and high LDL cholesterol.[8] Self-management program with the motivational interview was found effective in slowing down the pression of CKD in diabetes patients with stage 3 CKD as evidence with an increased in GFR, a persistent serum creatinine level, and a decrease in urine albumin.[9] In addition, HbA1C was negatively related with eGFR; the lower HbA1C could result in a lower serum creatinine level and an increase in GFR.[10] The Ministry of Public Health also passed a policy promoting the prevention of stage 1 – 3 CKD which could progress to ESRD requiring a nationwide high financial burden renal replacement therapy.[6]

With all circumstances elaborated above and a great concern on the foreseeable burden, we aimed to determine factors potentially affecting renal impairment progression among diabetes patients of Banna Hospital. With its community care orientation, the context of care of this community hospital could be different from other levels of care. Specifically, we aimed to investigate the effects of demographic characteristics, blood sugar level, blood lipid level, kidney function levels, health behaviors, and comorbidities on the GFR level as the indicator of renal impairment in CKD. Prevalence of CKD regarding chronic renal failure levels in diabetes patients was also determined. The findings could be used to predict the progression of CKD in individual diabetes patients at community hospital level. The prediction of such progression is of great importance since early stage CKD shows no obvious signs or symptoms. Early detection and prediction of CKD progression could prompt a timely referral to the tertiary care settings for kidney disease specialists.

Methods

In this retrospective study, secondary data of diabetes patients from the HOSxP database of Banna Community Hospital, Banna district, Nakhonnayok province, were used. Based on the data of 3,250 diabetes patients from 2016 to 2018, the sample was drawn using a systematic random sampling on an alternative hospital number (HN). The sample size was estimated based on Yamane's concept. With a finite study population of 3,250 patients and an error of 0.025, a sample size of 1,130 was required.

To be eligible, the patients had to have type 2 diabetes and in the diabetes clinic. They also needed to have screening for kidney function impairment and behavior practice data from the 3O2S form of the Ministry of Public Health. Patient records with a missing of any of the study variables mentioned above were excluded. As a result, 1,254 patients were obtained.

Study instruments

Data collection form consisted of five sections. In the first section, demographic characteristics were collected including gender, age, education level, occupation, and residence. The second part collected laboratory data including lipid profile (cholesterol, triglyceride, LDL and HDL), kidney functions (BUN, serum creatinine, eGFR), and glycemic control (HbA1C and FBS). In the third section, health behavior of the patient was collected using the 3O2S form of the Ministry of Public Health including diet, exercise, smoking, and moods.[11] The

frequency of practicing each behavior was graded into five levels of not practicing at all, 1 – 2 days/week, 3 days/week, 4 - 5 days/week, and 6 - 7 days/week. The fourth section collected the patient's illness including duration of diabetes since diagnosed and body mass index (BMI). In the last section, the patient's risk of chronic renal failure (CRF) was graded based on their GFR levels into CRF levels 1 (no CRF), 2 (low CRF), 3 (moderate CRF), 4 (severe CRF) and 5 (ESRD) for GFR of > 90, 60 – 89, 30 – 59, 15 – 29, and < 15 mL/min., respectively.

Statistical analysis

Descriptive statistics including frequency with percentage and mean with standard deviation were used for demographic and clinical characteristics of the participants. Three stepwise linear regression analyses were performed on GFR as a dependent variable and three sets of independent variables, specifically, 1) laboratory biochemistry factors, 2) health behavior factors, and 3) health status factors. All statistical significance was set at a type I error of 5% (or *P*-value < 0.05). Statistical analysis was conducted using a free statistical software program.[13]

Results

Of the 1,254 type 2 diabetes patients in the out-patient clinic of Banna Hospital, the majority were female (70.10%), in their 61 – 70 years of age (31.90%) with an average age of 62.57 (a range of 20 – 97 years), and general labors as their occupation (47.77%). Laboratory biochemistry factors are detailed in Table 1.

Table 1 Laboratory biochemistry factors of the participants (N = 1,254).

	Mean	Standard deviation	Max.	Min.
Serum total cholesterol (mg%)	193.81	44.59	398.00	90.00
Serum triglyceride (mg%)	161.73	76.25	803.00	37.00
Serum LDL cholesterol (mg%)	114.72	38.77	254.00	24.00
Serum HDL cholesterol (mg%)	46.74	15.00	114.00	10.00
Serum BUN (mg/dl)	16.23	7.86	85.00	4.00
Serum creatinine (mg/l)	0.93	0.55	11.10	.30
Serum glucose (mg/dl)	148.11	50.41	412.00	62.00
Hb A1c (%)	7.74	1.94	18.10	3.10

For health behaviors, the majority of participants practice 1) diet control on the intake and salt, sugar, and fat 3 days per weeks (29.19%), 2) consumption of fruit and vegetable of at least half a kilogram daily 3 days a week (48.25%), 3) exercise or continuous movement of the body to the exhaustion 3 days a week (40.59%), 4) no stress control by projecting a positive outlook on life (mood control) (99.36%), 5) no cigarette smoking or second-hand smoking (97.85%), and 6) alcohol or alcoholic beverage intake 3 days a week (39.79%) (Table 2).

Table 2 Health behaviors of the participants (N = 1,254).

Health behaviors	Practice level	N	%
Diet control on the intake and salt, sugar, and fat	No practice	95	7.58
	1 – 2 days / week	297	23.68
	3 days / week	366	29.19
	4 – 5 days / week	356	28.39
	6 – 7 days / week	140	11.16
Consumption of fruit and vegetable of at least half a kilogram daily	No practice	63	5.02
	1 – 2 days / week	275	21.93
	3 days / week	605	48.25
	4 – 5 days / week	273	21.77
	6 – 7 days / week	38	3.03
Exercise or continuous movement of the body to the exhaustion	No practice	175	13.96
	1 – 2 days / week	450	35.89
	3 days / week	509	40.59
	4 – 5 days / week	116	9.25
	6 – 7 days / week	4	0.32
Stress control by projecting a positive outlook on life (mood control)	No practice	1246	99.36
	1 – 2 days / week	6	0.48
	3 days / week	0	0.00
	4 – 5 days / week	0	0.00
	6 – 7 days / week	2	0.16
Cigarette smoking or second-hand smoking	No practice	1227	97.85
	1 – 2 days / week	22	1.75
	3 days / week	5	0.40
	4 – 5 days / week	0	0.00
	6 – 7 days / week	0	0.00
Alcohol or alcoholic beverage intake	No practice	382	30.46
	1 – 2 days / week	288	22.97
	3 days / week	499	39.79
	4 – 5 days / week	84	6.70
	6 – 7 days / week	1	0.08

The patients were diagnosed with diabetes for 9.23 years by average with the majority being diagnosed for 6 – 10 years (32.22%). By average they were overweight with a mean BMI of 25.69 kg/m^2 and a mean waist circumference of 33.85 inches (Table 3).

Table 3 Health status of the participants (N = 1,254).

Health status	Mean	S.D.	Max.	Min.
Duration of diabetes since diagnosed (yrs)	9.23	5.40	32.00	1.00
BMI (kg/m^2)	25.69	4.62	46.09	13.62
Waist circumference (inches)	33.85	3.44	52.00	22.40

Since Banna Hospital is a community hospital, the majority of the patients were classified as level 1 chronic renal failure

(CRF) (45.35%), followed by levels 2 (32.35%), 3 (19.01%), 4 (2.63%) and 5 (0.66%), respectively (Table 4).

Table 4 Prevalence of chronic renal failure (CRF) of the participants (N = 1,254).

Risk to CRF based on GFR	N (%)
Level 1: renal damage was found; GFR > 90 mL/min.	551 (45.35)
Level 2: renal damage was found with slight decrease of GFR; GFR 60 – 89 mL/min.	393 (32.35)
Level 3: renal damage was found with moderate decrease of GFR; GFR 30 – 59 mL/min.	231 (19.01)
Level 4: renal damage was found with severe decrease of GFR; GFR 15 – 29 mL/min.	32 (2.63)
Level 5: end-stage renal disease; GFR < 15 mL/min.	8 (0.66)

Based on stepwise linear regression analysis, GFR level was significantly negatively associated with serum creatinine level (B = -44.28), HbA1C (B = -1.08), and serum BUN (B = -0.49), and positively with serum HDL (B = 0.06) (Table 5). These 4 biochemistry factors could explain as high as 75% of the variance of GFR.

Table 5 Relationship between GFR and biochemistry factors by stepwise linear regression analysis of the participants (N = 1,254).

Variables	B	Std. Error	β	T	*P*-value
Constant	131.780	2.688		49.02	< 0.001
Serum creatinine (mg/dl)	-44.28	2.52	-0.587	-17.55	< 0.001
HbA1C (%)	-1.08	.211	0.453	-5.14	< 0.001
Serum BUN (mg/dl)	-0.49	.108	-0.154	-4.56	< 0.001
Serum HDL (mg/dl)	0.06	.029	-0.062	2.08	< 0.001
R^2 = 0.75, Adjusted R^2 = 0.445, F = 409.64, *P*-value < 0.001					

Regarding health behavior factors, only alcohol or alcoholic beverage intake was significantly negatively associated with GFR (B = -1.488) (Table 6). This single health behavior factor could explain 15% of the GFR.

Table 6 Relationship between GFR and health behavior factors by stepwise linear regression analysis of the participants (N = 1,254).

Variables	B	Std. Error	β	T	*P*-value
Constant	105.18	1.473		71.42	< 0.001
Alcohol or alcoholic beverage intake	-1.488	0623	-.098	-2.387	0.017
R^2 = 0.15, Adjusted R^2 = 0.008, F = 5.67, *P*-value = 0.01					

Regarding health status factors, GFR was significantly negatively associated with BMI (B = -0.407) and duration of diabetes diagnosis B = -0.377) (Table 7). These two health status factors could explain 19% of the GFR.

Table 7 Relationship between GFR and health status factors by stepwise linear regression analysis of the participants (N = 1,254).

Variables	B	Std. Error	β	T	*P*-value
Constant	94.47	3.633		15.05	< 0.001
BMI	-0.407	0.127	-0.136	-3.191	0.001
Duration of diabetes since diagnosed	-0.377	0.113	0.130	-3.323	0.001
R^2 = 0.19, Adjusted R^2 = 0.021, F = 12.12, *P*-value < 0.001					

In short, GFR level was significantly negatively associated with serum creatinine, HbA1C, serum BUN, alcohol or alcoholic beverage intake, BMI and duration of diabetes diagnosis, positively with serum HDL.

Discussions and Conclusion

Our study found that the decline of GFR in type 2 diabetes patients was associated with the increase in serum creatinine, HbA1C, serum BUN, alcohol or alcoholic beverage intake, BMI and duration of diabetes since diagnosed. This finding was consistent with the study of Zoppini et al where HbA1C was associated with eGFR.[10] They found that a well controlled HbA1C could result in a lower serum creatinine level, which meant a higher level of GFR. Our finding was also consistent with the study of Janjumras and Pipatsatitpong.[7] However, our study did not include uric acid and urine albumin creatinine ratio (UACR) as predicting factors since there was a limitation of laboratory data of uric acid and albumin in a certain portion of the patients. In addition, our study did not find that triglyceride and LDL cholesterol were associated with the decline of GFR which was different from the study of Wongprakob and Piyabunditkul where the two parameters were associated with the decline of GFR.[8] The study of Tattumlae also found that LDL cholesterol was also associated with the CKD progression.[14]

In terms of effects of health behaviors based on the 3O2S of the Ministry of Public Health on CKD progression[12], alcohol or alcoholic beverage consumption was the only one with significant association with the decline in GFR in type 2 diabetes patients. Our finding was different from previous studies. Mood management, exercise and proper diet were

found to associate with a slower rate of GFR decline in the study of Tattumlae[14], while noncompliance to diabetic drugs, herbal use, no physical exercise, obesity, stress, smoking, and alcohol intake were associated with the GFR decline among diabetes patients with stage 1 – 3 CKD in the study of Chailimlamontri and Kantachuwessiri.[15] In our study, compliance to diabetic medications was not examined.

For the health status factors, only duration of diabetes since diagnosed and BMI but not waist circumference were significantly associated with the decline in GFR. This was consistent with the study of Dejma and co-workers where duration of diabetes since diagnosed was able to explain 11.9% of the variance of kidney complications.[16] In the study of Laksawut, a duration of greater than 5 years since diagnosed with diabetes was associated with a 1.99-fold risk of kidney failure.[17] The study of Utsakarn and colleagues found that kidney failure progression was associated with duration of diabetes diagnosis.[18] The study of Dodhia also showed that a shorter duration of diabetes diagnosis was associated with a 2.08-fold higher eGFR.[5] The study on epidemiology of chronic kidney failure among diabetes patients in Thailand reported that the median times to progress to CKD from G1-G2, G2-G3a, G3a-G3b, G3b-G4, G4-G5 were 4.4, 6.1, 4.9, 6.3 and 9 years, respectively compared with 9.4, 14.0, 11.0, 13.8 and more than 14.3 years, respectively for other patients.[19] For BMI, Sungkhang and Wangkaew also reported that the risk of CKD in type 2 diabetes patients was increased 1.49 folds with those 1 unit of BMI.[20]

In terms of prevalence of CKD among type 2 diabetes patients, most patients were classified as stage 1 CKD. The number of patients with later CKD stages were fewer. This finding was as expected since the study setting is a community hospital where early stage of CKD could be expected and later stages should be referred to tertiary care settings.

Banna Hospital has developed a CKD clinic to slow down the progression of kidney disease in patients with kidney disease and those with the risk of CKD. Our finding could be useful in screening the early sign of kidney disease such as microaluminuria screening which could prompt the urgent need to for special care for kidney disease. The association of HbA1C which reflects glycemic control from the last three months and the progression of kidney disease could also be used to stimulate awareness about a restrict glycemic control among diabetes patients. A better glycemic control could slow down the progression of CKD based on the outcome indicator of less than 50% of the patients that are able to reduce the progression of CKD, specifically those entering stage 4 or 5 requiring CAPD or hemodialysis in tertiary care settings. However, a small number of stage 4 - 5 CKD were found in our study since they were referred back to community hospital for continuous care in addition to the dialysis at the tertiary care settings.[17] The stage 5 CKD patients were taken care by palliative care concept by community hospital.

Based on our findings and the context of community hospital, recommendations are as follows. More studies in diabetes patients with medications orther than anti-diabetic drugs and patients with other co-morbidities should be done to determine the outcomes. In addition, qualitative studies on health behaviors especially on self-care in diabetes patients to slow down kidney failure progression should be conducted. Such studies could also provide more understanding about patients with conflicting factors such as low HbA1C but positive alcohol intake.

In conclusion, more type 2 diabetes patients with stage1 CKD was found, with a fewer number of patients in later stages. The decline of GFR in type 2 diabetes patients was associated with the increase in serum creatinine, HbA1C, serum BUN, alcohol or alcoholic beverage intake, BMI and duration of diabetes since diagnosed.

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