Chapter 1

Introduction

1.1 Background

Gout is the most common inflammatory arthritis in adult men and in women after menopause (Hyon et al, 2004). It is caused by the buildup of too much uric acid in the blood. When uric acid levels in the blood are too high, it may form urate crystals and deposits in connective tissues, in the joint space between two bones, or in both (Weaver, 2008). Deposition of urate crystals leads to inflammatory arthritis, which causes swelling, redness, heat, pain, and stiffness in the joints. The arthritis may become chronic and cause joint to deform permanently (Smith et al, 2010). In addition, deposition of urate crystals in the renal tract may lead to impaired renal function (Obermayr et al, 2008). About 50.0 % of gout patients have renal impairment (Tausche et al, 2011). Therefore, the most dangerous disease for gout patients is acute arthritis and renal failure. Renal failure was found to be the cause of death among 18.0 % to 25.0 % of gout patients (Edwards, 2008). Early detection of CKD and management of its risk is very important. It will be helpful to prevent and slow the progression of renal disease (Locatelli et al, 2002).

The trends in the prevalence of gout have been increasing in both developed and developing countries (Weaver, 2008). In England, the prevalence of gout increased from 3.0 per 1,000 to 10.0 per 1,000 between 1970 and 1990 (Harris et al, 1995). In USA, it increased from 2.9 per 1,000 in 1990 to 5.2 per 1,000 in 1999 (Wallace et al,

2004). In UK, it increased from 9.5 per 1,000 in 1993 to 14.0 per 1,000 in 1999 (Roddy and Doherty, 2010).The increasing of gout prevalence among the Maori men in New Zealand rose from 82.0 per 1,000 in 1956 to 139.0 per 1,000 in 1992, and from 7.0 per 1,000 to 58.0 per 1,000 in European men (Klemp et al, 1997). In Taiwan in 1993-1996, the prevalence of gout among men and women increased from 47.4 per 1,000 and 21.9 per 1,000 to 82.1 per 1,000 and 23.3 per 1,000 respectively (Chuang et al, 2011). In China, the prevalence of gout increased from 3.6 per 1,000 in 2002 to 5.3 per 1,000 in 2004 (Roddy and Doherty, 2010). In addition, the prevalence of gout in Thailand in 1998 was 16.0 per 1,000 (Chaiamnuay, 1998). The increasing prevalence of gout may be related to several factors, including longevity, obesity, metabolic syndrome, hypertension (HT) and renal disease, increasing use of diuretics, as well as dietary trends (Klemp et al, 1997).

Gout has a definite impact on patients' health-related quality of life (HRQOL). When gout patients have renal disease, it makes patients' HRQOL worse (Hirsch et al, 2010).

Hyperuricemia was associated with an increased risk for developing CKD (Obermayr et al, 2008). Hyperuricemia was found in 90.0 % of gout patients and approximately half of them had impaired renal function (Kang and Nakagawa, 2005). So, the serious complication in gout patients is end stage renal disease (ESRD). According to Edwards et al, 2008 ESRD accounted for 18.0 % to 25.0 % of deaths among gout patients. Therefore, early detection of CKD and management of its risk factors are very important to prevent and slow the progression of CKD to ESRD (Locatelli et al, 2002).

Nongjik Hospital is a 30-bed community hospital in Pattani province, Southern Thailand. Gout is a common form of inflammatory arthritis in Nongjik. Chronic gout patients are usually treated by general practitioners (GPs). Gout medications comprise allopurinol and colchicine. All gout patients are prescribed the same drug dosage as those with normal kidney function. This study aims to investigate the prevalence of CKD and its risk factors: body mass index (BMI), hypertension (HT), diabetes mellitus (DM), dyslipidemia, thiazide use, antigout agent and serum uric acid associated with CKD among gout patients in Nongjik Hospital.

1.2 Objectives

1. To examine the prevalence of CKD among gout patients in Nongjik Hospital, Pattani Province
2. To identify the association between BMI, HT, DM, dyslipidemia, thiazide use, antigout agent, serum uric acid and CKD among gout patients in Nongjik Hospital

1.3 Expected advantages

The results from this study will be useful for early detection of CKD and the management of its risk factors among gout patients in Nongjik Hospital.

1.4 Literature review

1. The prevalence of CKD in gout patients

The prevalence of CKD in gout patients varies widely from country to country. The early studies of CKD were based on only the measurement of serum creatinine level. However, after 2002, most of the CKD studies were based on the estimation of glomerular filtration rate (eGFR) according to the National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF/K-DOQI) guidelines (National Kidney Foundation, 2002). A study in Taiwan (Chen et al, 2003) reported that CKD was found in 23.2% of 7,836 gout patients in the Ho-Ping gout database from 1983 to 1991 and in 18.4% of 19,354 gout patients from 1992 to 1999. In this study, CKD was defined as a serum creatinine more than 132.6 µmol/l or 1.5 mg/dl. The results of a study on the patients who underwent surgery for tophaceous gout at Middlemore Hospital, New Zealand from 1995 to 2001 (Kumar and Gow, 2002) revealed that the prevalence of CKD in 45 gout patients who had gouty tophi was 38.0%. In this study, CKD was based on serum creatinine more than 110 µmol/l or 1.2 mg/dl. In the UK and Germany, CKD was found in 9.5% of 7,443 gout patients in the UK and in 4.8% of 4,006 gout patients in Germany database of the IMS Disease Analyzer from 2002 to 2005 (Annemans et al, 2008). In this study, CKD was defined as a serum creatinine more than 150 µmol/l or 1.7 mg/dl.

Since 2002, the eGFR has been used for estimating the prevalence of CKD in gout patients. In the USA, CKD was based on eGFR < 90 ml/min/1.73m^2 (Fuldeore et al, 2011). CKD was found in 39.1 % of 3,929 gout patients in a managed care setting. More than half (67.2%) of the gout patients with CKD had CKD stage 2 (eGFR 60-

89), 23.2% had CKD stage 3 (eGFR 30-59), and 9.6% had CKD stage 4 or 5 of CKD (eGFR 15-29). Therefore, if based on eGFR < 60 ml/min/1.73m^2 according to the definition of CKD by the NKF/K-DOQI guidelines, only 12.8.0 % of gout patients had CKD. In addition, in France, CKD was reported in 43.0 % of 697 gout patients in Vivactis tudes cliniques (Courbevoie, France) from 2008 to 2009 based on estimated creatinine clearance (eCrCl) using the Cockroft-Gault equation (Liote et al, 2012). The eCrCl is useful for estimating the eGFR. There were 23.4% of gout patients with mild renal failure (eCrCl 60-80 ml/min), 18.2% with moderate renal failure (eCrCl 30-60 ml/min), 1.3% with severe renal failure (eCrCl 15-30 ml/min) and 0.1% with ESRD (eCrCl < 15 ml/min). Therefore, if CKD was based on eGFR less than 60 ml/min/1.73m^2, only 19.7 % of gout patients had CKD.

The calculation of eCrCl was based on the Cockcroft and Gault equation defined as follows:

$$eCrCl = \frac{(140 - age) \times weight(kg) \times 0.85(if\ the\ individual\ is\ female)}{72 \times serum\ creatinine}$$

2. The risk factors for CKD in gout patients

There is a lack of study on the risk factors for CKD in gout patients. A cross-sectional study in France found that sex, age, hypertension, diuretic use, and a history of obstructive nephropathy were significantly associated with CKD (Liote et al, 2012). DM type 1 or 2 was not significantly associated with CKD.

1.5 Scope of the research

This study focuses on outpatients who had diagnosis of gout (International Classification of Diseases (ICD 10) coded as "M10") in Nongjik Hospital during January 2004 to December 2010.

Definitions of terms

1. CKD is defined as eGFR less than 60 ml/min/1.73 m^2.
2. eGFR is the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule per unit time.
3. The stage of CKD is defined by the level of eGFR as follows:
   All patients with eGFR $\geq$ 90 ml/min/1.73 m^2 are defined as having no CKD. Patients with eGFR 60-89 ml/min/1.73 m^2 are assigned to the stage 2 (mild disease) category, eGFR 30-59 ml/min/1.73 m^2 are assigned to the stage 3 (moderate disease) category, eGFR 15-29 ml/min/1.73 m^2 are assigned to the stage 4 (severe disease) category and eGFR < 15 ml/min/1.73 m^2 are assigned to the stage 5 (Kidney failure) category.
4. Creatinine is a waste product of creatine, an amino-acid contained in muscle tissue and found in urine.
5. Uric acid is a waste product of purine metabolism.