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The Cost and Quality of Life of Malaysian Type 2 Diabetes Mellitus Patients with Chronic Kidney Disease and Anemia

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ABSTRACT

Background: Anemia is common among patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) and an independent risk factor for renal disease progression. Health economic evidence is important in Malaysia and yet cost and quality-of-life (QOL) data are scarce. **Objectives:** To investigate prevalence, factors associated with anemia, and cost and QOL among T2DM patients with CKD. Here, we present the estimated 1-year cost and QOL related to anemia in this group. **Methods:** A cross-sectional, observational study was performed at 20 government clinics. Treatment cost was calculated on the basis of resource utilization ascertained through data extracted from medical records and patient recall. QOL was elicited using the short form 36 health survey version 2 questionnaire. Propensity score matching was performed and costs and QOL were analyzed by anemia status and CKD stage. **Results:** Data for 816 patients were obtained. The propensity score matching enabled a comparison of 257 patients with and without anemia. Annual treatment costs were significantly higher for patients with anemia (Ringgit

Malaysia [RM] 4219 [US \$983] vs. RM2705 [US \$630]; $P = 0.01$). QOL scores were lower for patients with anemia but not statistically significant (physical component summary score: 44.8 vs. 46.2; $P = 0.052$; mental component summary score: 51.3 vs. 51.7; $P = 0.562$). Costs were higher and QOL lower among CKD stage 5 patients. **Conclusions:** This study was the first to examine anemia in this group of patients. Costs were significantly higher among anemic patients compared with nonanemic patients; patients with higher CKD stage 5 fared less well than did those in lower stages. This information suggests the need to increase detection, prevention, and early treatment of anemia when managing T2DM patients, particularly those with CKD.

Keywords: anemia, chronic kidney disease, cost, quality of life, type 2 diabetes mellitus.

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Introduction

Type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) are two common chronic diseases in Malaysia, a middle-income developing country. The burden of diabetes and its complications is increasing in this nation as in other developing countries because of changes in lifestyle and dietary habits associated with socioeconomic development [1]. The prevalence of T2DM has approximately tripled over the last three decades from 6.3% in 1986 to 17.5% of the adult population in 2015 [2]. Meanwhile, the prevalence of CKD in Peninsular Malaysia was high at 9.1% of the adult population in 2011. Among these, 4.2% patients were in CKD stage 1, 2.0% in CKD stage 2, 2.3% in CKD stage 3, 0.2% in CKD stage 4, and 0.4% in CKD stage 5 [3]. Diabetes is the leading cause of renal failure for patients commencing dialysis, increasing from 53% of new dialysis patients in 2004 to 61% in 2013 [4]. In a vicious cycle, CKD can give rise to other

complications such as abnormalities of bone metabolism, metabolic acidosis, malnourishment, and anemia [5].

Anemia is a common finding in diabetic patients with CKD [6] and is associated with left ventricular hypertrophy, congestive heart failure, as well as the typical complications of diabetes such as nephropathy, retinopathy, and neuropathy [7–10]. In patients with T2DM, it has been shown that the presence of anemia is an independent risk factor for progression of renal disease. In the Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study, the hazard ratio of end-stage renal disease was 4.23 for T2DM patients with low hemoglobin (Hb) (<11.2 g/dl) compared with those with normal Hb (>13.8 g/dl) [11]. A study from Hong Kong reported anemia prevalence of 22.8% among T2DM patients, with a significant increase in prevalence as renal function deteriorates [12]. In Iran, anemia prevalence was 19% among T2DM patients; those with moderate renal impairment had

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significantly higher prevalence (30%) compared with those with mild renal insufficiency (9%) [13].

Among patients in whom these conditions converge, it can be expected that the multiplicity of symptoms could give rise to worsened health-related quality of life (QOL). There were limited studies reporting on QOL on this topic, but two studies reflected poorer QOL of patients with anemia. A study in the United States and Canada among CKD stage 3 to stage 5 patients found a significant change in respondents' short form 36 health survey (SF-36) physical component summary (PCS) score according to serum Hb levels: lower levels of Hb corresponded to lower PCS scores (Hb <11 g/dl, PCS 37.1; Hb 11 to ≤12 g/dl, PCS 40.0; Hb 12 to ≤13 g/dl, PCS 38.3; Hb >13 g/dl, PCS 42.5; $P < 0.0001$) [14]. Nevertheless, there were no significant differences in mental component summary (MCS) score. Stevens et al. [15] found that subjective reporting of ill health among European diabetic patients was higher among patients with anemia (47%) than among those without anemia (28%). The study also found that a greater proportion of anemic patients (74%) reported tiredness and lethargy compared with nonanemic patients (52%).

In Malaysia, the cost of treating chronic diseases is largely borne by the government through subsidized health and medical services. In recent years, health economic analysis is increasingly being used in decision making. Nevertheless, patients too may have to shoulder the burden of costs in chronic and highly impactful diseases. In a study on cancer costs in the Association of Southeast Asian Nations region, patients and their families were shown to be greatly financially impacted [16]. Specific to anemia, past studies conducted in other countries have shown that anemia increases the cost of treatment. The cost of anemia among patients with CKD and T2DM has, however, not yet been reported. A study by Ershler et al. [17] using administrative claims data in the United States found that treatment costs for CKD patients with anemia (US \$78,209/y) were higher than for nonanemic patients (US \$24,784/y). Similarly, Lefebvre et al. [18] also using US claims data reported a significant increase of US \$1089 in the medical cost for elderly CKD patients ($P < 0.0001$) during periods when these patients had anemia. Also using US claims data, Chaves et al. [19] reported that patients with chronic anemia had significantly higher rates of hospital admission (0.31 vs. 0.09 admissions per year; $P < 0.001$) and longer length of stay (5.08 vs. 3.68 days per admission; $P < 0.001$) than did patients without anemia. The mean annual cost for patients with anemia was also higher than the mean annual cost for those without anemia (US \$11,078 vs. US \$5,968; $P < 0.0001$).

Thus far, there has been no study conducted in Malaysia or in any other country on all three comorbid conditions existing in parallel. Past QOL studies have been focused on only one of the primary conditions of interest among diabetic patients [20,21], dialysis patients [22,23], and CKD patients [24]. Previous cost studies were limited to the cost of diabetes [25,26]. In view of the high prevalence of T2DM and the etiological link between T2DM and CKD, we performed a study with the primary objective of estimating the prevalence of anemia in the presence of both T2DM and CKD. Its secondary objectives were to examine factors associated with anemia, and the cost and QOL of patients with anemia. In this article, we present the estimated 1-year cost and QOL related to anemia in this group of T2DM patients with CKD in Malaysia. The findings on anemia prevalence and factors associated with anemia are reported elsewhere.

Methods

Study Design and Population

We performed a cross-sectional observational study of Malaysian T2DM patients visiting government health clinics. Patients with

T2DM and CKD were recruited at 20 participating health clinics in Peninsular Malaysia from October to December 2015. Every third patient with T2DM registering at the study site for that particular day was screened for inclusion and exclusion criteria. Inclusion criteria were male and female subjects, aged 18 years and older, diagnosed with T2DM and CKD between stages 1 and 5 according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative classification [27]. Patients were excluded if they were pregnant, postpartum within a period of less than 3 months, or had an established diagnosis of anemia secondary to a blood disorder (e.g., thalassemia) or any history of psychiatric illness. All study procedures were performed at the same visit with the data recorded in a case report form. Patients were asked about their history of hospitalizations, blood transfusions, major cardiac procedures, and outpatient clinic visits to specialists and primary care within the past 1 year. Data on currently prescribed drugs were extracted from medical records.

The primary outcome measure was anemia defined according to the Kidney Disease Outcomes Quality Initiative guideline of Hb level of less than 12 g/dl for women and less than 13 g/dl for men [28]. The Hb value used to determine current anemia was the most recent Hb test value available for the study subject, provided the Hb test was performed within the 6 months before the date of study data collection. Patients who did not have a test performed in the past 6 months underwent a blood test to determine their Hb level.

Some patients were categorized as having “corrected anemia.” This was defined as a normal Hb on the latest Hb test, but the patient had a history of anemia that was corrected by being given appropriate treatment (e.g., iron, vitamin B₁₂, folate, folic acid, or erythropoietin). In the cost analysis, patients with current anemia and those with corrected anemia were categorized as being anemic. Because QOL status was elicited on the day of the study visit, in the QOL analysis, patients with corrected anemia were considered to be nonanemic to reflect their current serum Hb level.

Patients' QOL status was obtained through self-administration of validated versions of the SF-36 version 2 (SF-36v2) QOL instrument in English or Bahasa Melayu [29]. The SF-36 measures QOL according to eight health domains (physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health) and summarizes QOL in terms of two summary measures (PCS and MCS scores) [29]. The scaled score for each domain is converted to a 0 (worst health) to 100 (best health) scale. Both component scores have a mean score of 50, approximating the average physical and mental QOL of the general population [30].

Initial analysis of the full study sample of 808 observations indicated that the distributions of T2DM and CKD durations between patients in the anemic and the nonanemic groups were very different. Therefore, propensity score matching was used to overcome the problem of bias within each group caused by confounding variables [31]. Various combinations of confounders were tested, with the final matching done using propensity scores for age, duration of T2DM, duration of CKD, and the number of comorbidities used as matching variables. Nearest neighbor matching without replacement was used as a matching estimator between anemic and nonanemic patients.

Cost Analysis

An estimation of medical costs was necessary because Malaysian government health facilities are heavily subsidized and the actual charges incurred by patients do not reflect the economic cost of resources used to provide care. In this study, to estimate the cost of medical care, the 1-year cost of managing all patients in the study was estimated on the basis of resource utilization

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