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Research Article

Health utility score in type 2 diabetes mellitus

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ABSTRACT

Cost-utility analysis requires data of severity-based health utility score for calculating the Quality adjusted life years. This study aims to figure out utility scores based on complications, comorbidities and diabetes treatments in patients with type 2 diabetes mellitus.

The study was conducted using cross-sectional design in patients with type 2 diabetes mellitus who visited regional hospitals in Yogyakarta, Indonesia. Utility score was measured using EQ-5D-5L questionnaire. The scoring was performed using a value set developed for the Indonesian population.

The results of the study in 418 patients with diabetes mellitus with an average age of 60.74 (SD=8.61) years showed that the utility score and the average Visual analog scale (VAS) value were 0.74 (SD=0.22) and 74.60 (SD=12.23) respectively. Problems related to the mobility were reported in 42.67**%** of the patients, while for self-care domain in 11**%** , daily activity in 48**%** , pain/uncomfortable in 76.33**%**, and anxiety/depression in 44.33**%**. There were significant differences in the utility score based on complications related to DM, that the mean utility score of DM patients without complications was 0.79 (SD=0.16), with microvascular complications was 0.76 (SD=0.19), with macrovascular complications was 0.71 (SD=0.19) and with microvascular and macrovascular complications was 0.59 (SD=0.31). The lowest utility score was in the patients with stroke complications by 0.43 (SD=0.32). The differences in the therapeutic regimens given also indicated the different utility scores. Diabetes mellitus patients with complications showed lower utility scores. Health utility scores based on complications could be used as a supporting data in the pharmacoeconomic analysis.

1. INTRODUCTION

Cost-utility analysis (CUA) is a method that is widely used to assess the value of health intervention. CUA uses to compare costs and QALYs of at least two interventions, which is presented as incremental cost-effectiveness ratio (ICER). The numerator of ICER is an additional cost of intervention and the denominator shows a Quality adjusted life years (QALYs) or incremental health benefit[1].

QALYs combines the health-related quality of life (HRQoL) and the length of life in a single measurement index. The HRQOL is described as the quality weights (utilities) which are measured on a scale of 0 to 1, whereas 0 is defined as the health status equivalent to mortality, and 1 is the full health. Health utility.

score can be assessed by using standard gamble, time trade-off, visual analog scale, ranking exercise, and discrete-choice experiment in order to combine the quality of life and the length of life into one measure. Nevertheless, there are limitations in practice, reference values for the utility on the special health states are often used when the quality of life evaluations are required[2].

A valid utility estimate is an important parameter for CUA. QALY which combines mortality and Health-related quality of life (HRQoL) with a single measure and is recommended as the most preferred method for measuring health effects. However, utility estimates vary greatly depending on many factors such as research design, preference elicitation method, health status classification instrument, population and value set. A consistent approach to the scoring utility method is important to ensure that the method used is appropriate and comparable among several studies. For example, NICE and the Panel on cost-effectiveness in health and Medicine in the United States (US) adopt the use of a reference case to facilitate a consistent method. NICE also uses the EuroQol five-dimensional questionnaire (EQ-5D) scores. A single-source catalogue of nationally representative EQ-5D estimates has been published for a chronic disease in the US and United Kingdom (UK) in the Medical expenditure panel survey data[3].

Diabetes mellitus does not only increase morbidity and mortality, but also increases a perception of the quality of life. In addition, the complications of DM can decrease the quality of life. Several studies show that the incidence of diabetic complications indicates to have a significant impact on the quality of life. Moreover, the quality of life of patients who are newly diagnosed with diabetes and patients with impaired glucose tolerance also decrease[4]. One aspect that can worsen the clinical outcome of diabetes is the development of diabetes-related comorbidities. There have been many researches about the quality of life of patients with DM conducted in Indonesia using various instruments, either specific instruments such as diabetes quality of life clinical trial and diabetes quality of life questionnaire, or even generic instruments namely Short Form-36, Short form-6 dimension, and World health organization-quality of life BREF. This research is done to assess a utility using EQ-5D-5L instruments in Indonesian version, and to score the utility index using the value set which is developed based on the Indonesian population. This research aims to estimate the utility score on diabetic patients, complication related to DM, as well as to find out the utility score difference based on the patients' socio-demography.

2. MATERIALS AND METHODS

The target population in this study was type 2 DM patients who visited regional hospitals (three hospitals) in Yogyakarta, Indonesia. The diabetic patients who are eligible to participate in this research should be at least 18 years old, able to speak bahasa Indonesia, are not pregnant, and have been having DM for at least a year and have received the antidiabetic.

Demographic data of the patients were obtained from their medical records including age, gender, education level, body mass index, duration of diabetes, HbA1c, comorbidity, complications of diabetes and therapeutic regimen. Education level was categorized into a low level of education (primary or not attending formal school), secondary (junior, high school or equivalent) and tertiary (college or equivalent). BMI was categorized as underweight, normal, overweight, and obese. Therapy with antidiabetic was categorized into three, namely therapy with oral medication, insulin alone and a combination of insulin and oral medication. Meanwhile, the complications in this study included stroke, cardiovascular disease, ulcus diabeticum and peripheral vascular disease, chronic kidney disease, neuropathy and retinopathy.

HRQoL was assessed using the EQ-5D-5L, a multi-attribute instrument for measuring preferences related to health states in individuals. The instrument consisted of a visual analog scale (VAS) and a descriptive system with 5 dimensions (mobility, self-care, usual activity, pain/discomfort, anxiety, and depression) and 5 levels (no problem, slight problem, moderate problem, severe problem, and extreme problems). Patients were given an EQ-5D-5L questionnaire at the time of visiting the hospital. Scoring was performed using the value set for the Indonesian population with a range of 0 (worst state of health) to 1 (best state of health) [5]. In order to find out factors affecting HRQoL, this study employed to find out the utility score differences based on gender, the independent t test is used. While to find out the utility score differences based on age, level of education, body mass index, duration of having the diabetes, and antidiabetic therapy, the Annova test is used.

Table 1. Characteristics of type 2 diabetes mellitus patients

Patients (N)	418
Age (years)	60 (27 – 87)
Female	58.9%
Education (%)	
< High school	22.0
High school graduate	50.5
> High school	27.5
Current/ever smokers (%)	14.4
Diabetes duration (years)	9.78 (0.25 – 40)
HbA1c (%)	8.49 (5.4 – 14.3)
Diabetes treatments (%)	
Oral medication	38.5
Insulin	28.7
Insulin and oral medications	32.8

This research has been approved by the Ethics Committee of the Medical Faculty of Universitas Gadjah Mada Yogyakarta, with the numbers of KE/FK/0790/EC/2017.

3. RESULTS

The study on 418 patients with diabetes mellitus showed an average age of 60.65 years with an age range of 27 to 87 years, 58.9**%** of women with an average diabetes duration of 9.78 years (4 months-40 years), and 61.5**%** of patients with hypertension (Table 1).

The results of the observations with the EQ-5D-5L questionnaire showed that 39.5**%** of the patients experienced pain/discomfort slight problems and 31.6**%** reported slight problems associated with daily activities and 25**%** reported slight problems associated with anxiety/depression. Only 6**%** of the patients reported slight problems associated with self-care (Table 2).

The average utility score in 418 diabetic patients was 0.74 (SD=0.22) and the VAS value was 0.746 (SD=0.12). The sociodemographic factor related to the quality of life was the level of education (p=0.013). Based on the diabetes treatments, patients with insulin therapy showed the lowest health utility score (0.71). Patients with a combination of insulin therapy and oral antidiabetic showed the highest utility score (0.81). Patients with microvascular and macrovascular complications showed the lowest utility scores, that was 0.69 (SD=0.24). In patients with microvascular complications, their utility scores were 0.72 (SD=0.20) lower than patients with microvascular complications (0.76) (Table 3).

4. DISCUSSION

Diabetic patients did not only have shorter life expectancy than non-diabetic patients, but also had lower HRQoL. In other words, diabetic patients with complications had lower HRQoL than those without complication. In the economic model, HRQoL was an important parameter, while health states were an important aspect in cost-effective therapy. From health economic perspective, preference-based measure HRQoL was needed for the health-state utility value estimates and to calculate QALYs.

The results of this study showed that 73.9% of the patients experienced pain/discomfort problems, consistent with a study on 3,089 patients with diabetes mellitus in Sweden which showed that the highest prevalence of moderate and severe problems reported by the patients were pain/discomfort (55.5%) and the lowest was self-care (5.5%)[6]. Janoo et al. (2017) reported that HRQoL was associated with diabetes self-care activities. In addition, dimensions of the EQ-5D index were significantly influenced by non-adherence to foot-care, duration of exercise, and smoking. The results showed that adherence was

Table 2. EQ-5D-5L distribution of the patients with Type 2 Diabetes Mellitus (n=418)

	Mobility	**Self-care**	**Usual activities**	**Pain/ discomfort**	**Anxiety/ depression**
No problems	59.6%	90.7%	58.1%	26.1%	58.9%
Slight problems	21.3%	6.0%	31.6%	39.5%	25.6%
Moderate problems	16.5%	2.6%	8.9%	29.4%	12.9%
Severe problems	2.4%	0.5%	1.0%	4.8%	2.6%
Extreme problems	0.2%	0.2%	0.5%	0.2%	0%

Table 3. Unadjusted EQ-5D-5L health utility score by patient characteristics

Characteristics	% n=418	EQ-5D-5L score Mean (SD)	P-value
Age (years)			
≤ 44	3.6	0.73 (0.19)	0.280*
45 – 64	62.4	0.77 (0.22)	
> 65	34	0.73 (0.21)	
Gender			
Female	58.2	0.76 (0.21)	0.789**
Male	37.1	0.76 (0.26)	
Education			
< high school	22	0.68 (0.25)	0.013*
High School graduate	50.5	0.78 (0.24)	
> High School	27.5	0.81 (0.18)	
Body mass index (kg/m^2)			
18.5 – 24.9	34	0.76 (0.22)	0.866*
25 – 30	23.7	0.75 (0.25)	
> 30	42.3	0.76 (0.19)	
Time since diagnosis (years)			
< 5	25.4	0.75 (0.25)	0.135*
5 – 10	38	0.78 (0.18)	
> 10	36.6	0.74 (0.23)	
Diabetes treatments			
Oral medication	38.5	0.77 (0.23)	0.050*
Insulin only	28.7	0.71 (0.27)	
Insulin and oral medication	32.8	0.81 (0.19)	
Hypertension	61.5	0.73 (0.23)	N/A
Hyperlipidemia	31.8	0.75 (0.21)	
Complications			N/A
Stroke	5.5	0.49 (0.34)	
Cardiovascular disease	13.6	0.73 (0.21)	
Ulcus/Periferal disease	6.5	0.62 (0.22)	
Chronic kidney disease	24.6	0.69 (0.26)	
Neuropathy	34.2	0.73 (0.22)	
Retinopathy	1.4	0.56 (0.29)	

an important determinant of diabetes-specific distress. Diabetes self-care activities also reduced distress and improved the quality of life[7].

41.9% of the patients reported problems associated with anxiety/distress. A research in 213 diabetic patients in Singapore showed a poor glycemic control caused by diabetes-related distress and HRQoL. Psychological distress was a mediator of the relationship between glycemic control and HRQoL. In the context of diabetes, the form of diabetes distress was categorized into two, namely major depressive disorder (MDD) and diabetes-related distress (DRD). MDD was caused by clinical depression, sadness, frustration, anxiety and negative mood. DRD was a distress due to the burden of life with chronic diseases, such as difficulty in adjusting to social situations (with healthcare provider, family and/or friends), therapeutic regimens, and diets. The results showed that glycemic control was only caused by DRD and not caused by MDD. Ang Co reported that the effects of DRD on the glycemic control were through changes in healthcare behaviors such as poor physical activity, poor diet, and non-adherence to treatment which could contribute to the increased visceral adiposity and increase the insulin resistance, thus exacerbating the blood glucose control[7].

The result of Clarke's study showed the utility scores in patients with diabetes was 0.77 (SD=0.27) and an average VAS score was 0.74 (SD=0.19), while the study of Nejhad et al. (2013) in 3472 diabetic patients in Iran showed the average HRQoL score using EQ-5D visual analog scale was 56.7 (20.7). This HRQoL score was lower than that of utility scores in patients with DM in the US. The averages of EQ-5D of patients with diabetes mellitus in US, UK, France and Spain were 0.792, 0.719, 0.700 and 0.759, respectively[7].

The results of this study showed that the utility score of patients with uncomplicated diabetes was 0.82 (SD=0.20). Glasziou et al. reported that a health utility score in diabetic patients without complication was 0.88 and Hayes et al. reported that an average health utility score was 0.827 (95% CI 0.824-0.830)[8]. Kiadalri et al. reported that the average of the EQ-5D

index in diabetes patients without complication in the UK was 0.79, the score was the same as it was reported in the UKPDS 62 study, which was 0.79 lower than that of diabetic patients in Norway (0.85). A decrease in the utility index was due to the complications varying from 0.012 to 1.114 if using a value set from the UK and a range of 0.010 to 0.059 with a value set from Swedish[6]. Meanwhile, the utility index in Canada was 0.046–0.102 and in the US was 0.012–0.108. Differences in patient characteristics, clinic settings, range of complications and statistical analysis methods contributed to the different utility scores. In addition, the diagnostic methods influenced the HRQoL scores, where the quality of life of patients who were identified in screening programs or patients who performed medical checkups was better than those who were diagnosed because of having symptoms.

Nejhad et al. (2013) reported that many factors were affecting the quality of life in patients with DM, including ethnicity, race, socioeconomic status and diabetes complications[11]. Imayama et al. (2011) conducted a study of determinant factors of quality of life in diabetic patients over 18 years of age. The results of the study showed that the income per year, socioeconomic status and age greatly affected the quality of life[9]. Low socioeconomic status was caused by mortality, progression of type 2 DM and cancer[10]. The results of this study were also consistent with the research of Nejhad et al. (2013) that HRQoL was influenced by education, while the other factors affecting HRQoL were gender, duration of diabetes, diagnostic methods, occupation and number of visits to the health facilities[11]. Nutrition, access to better quality healthcare and counseling had a significant effect on the blood glucose control. The limitations of social relationships and disability also affected the HRQoL[12]. Based on body mass index, underweight patients showed the lowest utility score (0.69), while the utility score of patients with BMI $\geq$ 30 was 0.74. Hunger et al. reported that BMI was significantly associated with health utility score even after adjustment for macro- and microvascular complications[13]. The results of this study were consistent with the research from Zhang et al. that patients with BMI $\geq$ 35 kg/m2 (obese) had lower utility scores. Obesity could affect physical functioning, decrease energy, improve distress and decrease self-rated health[14].

Patients with a combination of insulin therapy and oral antidiabetic showed the highest utility score (0.81). Huang et al. research showed the different results that a comprehensive therapy had a negative effect on QoL than a conventional therapy. Patients with a comprehensive therapy used a combination of therapy with anti-hyperlipidemia, aspirin, intensive blood pressure control (two to four antihypertensive drugs) and intense blood glucose control (oral antidiabetics combination and insulin). Therapy-related QoL would improve if the therapeutic regimen could be simplified or modified through therapeutic innovation. Therefore, new treatment modalities should focus on patient' s QoL. For example, dipeptidyl peptidase-4 inhibitors did not only improve glycemic control, but also the blood pressure, lipid profile, and QoL. Scunk et al. reported that therapeutic regimen was related to the progression of diabetes, where the patients were given intensive therapy such as combination therapy or insulin therapy, risk of worse glycemic control and complications of diabetes. However, the results from the previous studies were inconsistent that the insulin therapy had better HRQoL after adjustment for comorbidity[15].

The research results from Zhang et al. (2012) showed that therapy with insulin significantly decreased the utility, but it was not known whether the low utility scores associated with insulin use did not improve functional capacity or because insulin therapy was administered related to the diabetic severity[14]. Patients with insulin were patients with longer duration of diabetes and having more complications than those with oral antidiabetics. In addition, the use of insulin could lower the QoL because it directly caused discomfort and unwanted effects with injection, as well as hypoglycemia or indirectly made the stigma of the patient because diabetes could not be controlled. On the other hand, the use of insulin could improve the quality of life because the control of the glycaemia became better.

The results of this study showed that the glycemic control had a significant effect on HRQoL (p=0.019). Diabetic patients with better glycemic control demonstrated higher HRQoL. The main goal of diabetes therapy management was to achieve a range of HbA1c <7%. However, the variety and complexity of therapy could affect the HRQoL. The study of Dogan et al. (2016) showed a negative correlation between range of HbA1c and values of physical component summary (PCS) and mental component summary (MCS)[4]. Some studies have shown inconsistent

results that glycemic control was associated with better HRQoL, while other studies showed that there were a low correlation and no correlation of glycemic control with HRQoL. HRQoL was influenced by several factors including other health problems, socio-demography, knowledge, education, therapeutic satisfaction and family history of diabetes[16,17]. Kamarul et al. reported that in patients with poor glycemic control, there was a low HRQoL, but HbA1c was only categorized as good (range of HbA1c $\leq$ 7.5%) and poor (range of HbA1c $\geq$ 7.5%)[18]. A research of Sundaram et al. using the Short-Form 12 questionnaire showed that there was no association between HbA1c and QoL, but with the Audit of Diabetes-Dependent QoL, it showed that there was a low correlation[19].

The result showed that there was a significant correlation between complications and HRQoL. The systematic reviews of 21 studies in Europe, Asia, America and Australia showed a health utility score in patients with diabetes mellitus ranging from 0.711 to 0.94. The recommendation of the utility score of diabetic patients was 0.785. The largest decrease in the utility score was patients with peritoneal dialysis (-0.204) followed by active ulcer (-0.170), hemodialysis and stroke (-0.164)[20]. The results of this study were consistent with the previous studies that patients with stroke complications showed low utility scores of 0.49 and 0.69 in patients with chronic kidney disease. Clarke et al. assessed the utility score in 3,192 male diabetic patients without complications, i.e. 0.850 – 0.962. Estimates of decreased utility scores due to the complications were ranging from 0.055 to 0.280. Diabetic patients with neuropathic complications who performed amputations on both legs showed the lowest utility, i.e. 0.67, as well as the utility score of stroke patients with hemiplegia and diabetic patients with complications of kidney diseases who were performed dialysis was 0.68[21].

Clarke conducted a study in 645 diabetic patients that 556 patients had at least one complication. The highest complication was a myocardial infarction (6.2%). Macrovascular and amputation complications had negative effects on both utility and VAS scores, while blindness had significant negative effects on the utility scores. In patients without complication, the utility score was 0.785 and the VAS value was 0.747[2]. The difference in the utility scores was due to the wide range of diabetes treatments, complications, comorbidity and duration of diabetes. The utility scores estimate in this study used the value set developed for the Indonesian population, in contrast to the value sets used in other countries.

Limitations in this study included the design used, which was cross-sectional, so that the causality was not known. The measuring instrument used was a EQ-5D-5L, so that it was less specific for measurements in patients with diabetes mellitus, complications related DM, and elderly patients. Confidence intervals indicated a wide range, so that more samples based on each category of the variables analyzed were required. In addition, the severity of diabetic complications also affected the utility scores.

5. CONCLUSIONS

This study concluded that the differences in the diabetes treatments indicated the different utility scores. Diabetes mellitus patients with complications showed lower utility scores. Health utility scores based on complications that occurred could be used as supporting data in the pharmacoeconomic analysis.

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Conflict of interest

We have no conflicts of interest related to this work.

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Ethical approval

This study has been approved by the Ethics Committee of Faculty of Medicine of Gadjah Mada University with number KE/FK/0930/EC/2018.

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