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# Characteristics, Antihyperglycemics Utilization, and Quality of Life in Patients with Type 2 Diabetes Mellitus Admitted to a Primary Health Center

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> Abstract. This study aimed to assess the characteristics, utilization of antihyperglycemic drugs, and to analyze the quality of life (QOL) in type 2 diabetes mellitus (T2DM) patients. This two-month prospective descriptive cross-sectional study was undertaken by distributing the European Quality of Life - 5 Dimensions 3 Level (EQ-5D-3L) questionnaire to the patients with T2DM (n=50) admitted to Helvetia primary health center Medan to assessed their QOL. The patients' characteristics and the utilization of antihyperglycemic drugs were assessed from the patients' medical records using a self-designed questionnaire. The inclusion criteria were T2DM patients with age of 18 years or older, had no mental disorders, and agreed to sign the informed consent. The patients' characteristics, their OOL, utilization of antihyperglycemic drugs, and association among their characteristics and OOL were analyzed using descriptive and Chi-Square tests. All analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) (p value <0.05 was considered significant). It was found that the mean age of the T2DM patients was  $59.70 \pm 10.44$  (years). Most (66%) of them were females. Majority (80%) of the patients graduated from primary to senior high schools. Nearly half (44%) of the patients was provided glibenclamide. The mean QOL of the patients was  $0.79 \pm 0.14$ . There was no significant association between the patients' QOL and their characteristics (p values >0.05). This study proved that most of the T2DM patients were females. Glibenclamide was the most frequently prescribed drug for the patients. The QOL of the patients was 79% of full health.

Keyword: Antihyperglycemic Drugs, EQ-5D, QOL, T2DM

Abstrak. Penelitian ini bertujuan untuk mengakses karakteristik, penggunaan antihiperglikemia, dan menganalisis kualitas hidup atau quality of life (QOL) penderita diabetes mellitus tipe 2 (T2DM). Studi prospective descriptive cross-sectional ini dilakukan dengan mendistribusikan kuesioner the European Quality of Life - 5 Dimensions 3 Level (EQ-5D-3L) kepada pasien T2DM (n=50) yang berobat selama periode 2 bulan ke Puskesmas Helvetia Medan untuk memperoleh QOL pasien. Karakteristik dan pola penggunaan antihiperglikemia diakses dari rekam medik pasien menggunakan kuesioner yang didesain sendiri. Kriteria inklusi yaitu penderita T2DM umur 18 tahun atau lebih, tidak ada ganguan mental, dan setuju menandatangani informed consent. Karakteristik dan QOL pasien, pola penggunaan obat, serta hubungan antara karakteristik dengan QOL pasien dianalisis secara deskriptif dan tes Chi-Square. Semua analisis dilakukan menggunakan Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) (p value <0.05 dinilai signifikan). Hasil penelitian membuktikan bahwa usia penderita T2DM tersebut adalah 59.70 ± 10.44 (tahun). Sebagian besar (66%) dari pasien adalah perempuan. Mayoritas (80%) dari pasien berpendidikan sekolah menengah pertama dan sekolah menengah atas. Hampir setengah (44%) dari pasien diberi

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glibenclamide. Nilai QOL pasien adalah  $0.79 \pm 0.14$ . Tidak ada hubungan yang signifikan antara QOL dengan karakteristik pasien (p>0.05). Penelitian ini membuktikan bahwa umumnya penderita T2DM adalah perempuan. Glibenclamide paling banyak diresepkan untuk pasien T2DM. Kualitas hidup pasien tersebut mencapai 79% dari sempurna.

Kata kunci: Antihiperglikemia, EQ-5D, QOL, T2DM.

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## 1. Introduction

Diabetes mellitus (DM) remains as a global public health problem with continued increasing prevalence in developed as well as developing countries, including Indonesia. The disease contributed to 1.5 million of deaths worldwide in 2012. According to World Health Organization (WHO), the global prevalence of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in 2014. The number of adults with DM in 2014 reached 422 million compared to those in 1980 was only 108 million. In Indonesia, it was found that 99,400 incidences of death in patients with diabetes out of 258 million of the population. The disease contributed to 6% of the overall mortality in 2014 [1].

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia associated with abnormalities in the metabolism of carbohydrates, fats and proteins caused by decreased insulin secretion, decreased insulin activity or both which ultimately causes multiple medical complications, including nephropathy, retinopathy with potential blindness, neuropathy, gastrointestinal symptoms, amputation, impotence, symptomatic hyperglycemia, and hypoglycemia [2]. These conditions have resulted in reduced QOL and work productivity, which even finally leads to lower life expectancy. The disease will accompany the patient's lifetime and worsen over time if not treated properly[3]. Many complicated factors are associated with the QOL in patients with T2DM including age, gender, educational level, socioeconomic status, the disease duration, long-term multiple complications of DM, ability of the patients to cope with her or his diseases, and the provided health cares. These issues are the challenges of the health care systems in the international as well as national level[4, 5].

Varieties of health care programs in the management of DM have been implemented in different parts of the world. Yet, the health care programs should always be evaluated, analyzed, and improved in optimizing the scarce health resources and the public demand for health services. A pharmacoeconomic study plays a crucial role to evaluate the health care programs in the treatment of DM. One of the most important issues in this area is how to measure, value and incorporate changes in QOL into the economic evaluation. Therefore, the QOL as an outcome measure in the management of patients with T2DM must be studied [6].

Many studies on QOL in T2DM patients with different methods and extents have been undertaken by researchers elsewhere. A large scale study had been undertaken to characterize the impact of hypoglycemia on diabetes burden, QOL, and work productivity from the patients' perspective. This study indicated that hypoglycemia negatively impacts social function, overall QOL, and work productivity [3]. Another study on QOL using WHO Diabetes Treatment Satisfaction Questionnaire (DTSQ) in patients with T2DM (n=180) conducted in a primary health center in Turkey found that their score was  $21.02 \pm 8.07$  (range from better to worse: 36 to 0) for the entire group [7]. Additionally, in a cross-sectional study, QOL of 183 patients with T2DM was analyzed using a questionnaire called the Audit of Diabetes Dependent Quality of Life (ADDQoL). It was indicated that the mean score of the patients' QOL was  $0.98 \pm 0.89$  [8]. The characteristics of the patients with T2DM vary from one country to another due to differences in social economics status and health care systems which ultimately require different policies and approaches to optimize the disease management.

In relation to the problems previously described, the present study was undertaken to assess the characteristics, utilization of antihyperglycemic drugs, and QOL inT2DM patients admitted to Helvetia primary health center.

#### 2. Methods

This two-month prospective descriptive cross-sectional study was undertaken to access the characteristics, utilization of antihyperglycemic drugs and the QOL of patients with T2DM (n=50) admitted to Helvetia primary health center in Medan. This health center is included into one of the big five health centers with high patients' admission in this city. Thus, this center was chosen as the location of the study. The target population in this study was all patients suffered from T2DM admitted to Helvetia primary health center period June-July 2015. Patients with T2DM age 18 years or older, showed no mental disorder, and agreed to sign the inform consent were included into this study. The study was approved by Health Research Ethical Committee, Faculty of Medicine, University of Sumatera Utara, Indonesia. A self-designed questionnaire was used to access the patients' characteristics including gender, age, education, occupation, duration of the disease, complications and utilization of antihyperglycemic drugs from the patients' medical records. The QOL of each of the patients was assessed using EQ5D3L questionnaireas an instrument filled out by the patients with T2DM under the direction of the researchers [9]. The QOL of the patients assessed consisted of 5 dimensions including the patients' mobility, self care, usual activity, pain/discomfort and anxiety/depression). Each of the 5 dimensions was categorized into 3 levels known as 3L ( $1 = n_0$  problem, 2 = there is a bitproblem, and 3 = there is a serious problem). The preferences of each patient were expressed as index value ranging from 11111 (full health or 100%) to 33333 (worst health or zero) using the EQ5D value set [9]. The patients' characteristics and mean value of their QOL were descriptively analyzed. The scores of the patients' QOL were categorized into three grades

 $(\geq 0.8 = \text{good}, < 0.8-0.6 = \text{fair}, < 0.6 = \text{bad})$ . Association among their characteristics and their QOL were analyzed using cross-tabulation Chi-Square test. All analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 19, Chicago, IL, USA) (p value <0.05 was considered significant).

## 3. Results

In this study, there were 50 patients with T2DM recruited from the Helvetia health center period June-July 2015 that met the inclusion criteria. Characteristics of the patients with T2DM admitted to the primary health center are shown in Table 1. The mean age of the T2DM patients was  $59.70 \pm 10.44$  (years). Most of them (66%) were females, whereas only 34 % of them were males.

		Percentage (%)
Gender	Females	66
	Males	34
Age (years)	36-45	8
	46-55	28
	56-65	32
	>65	32
Education	Primary school	28
	Junior high school	22
	Senior high school	30
	University	20
Occupation	Housewife	48
_	Pensionary	20
	Enterpriser	18
	Official	8
	Teacher	6
Duration of the disease	≤10	70
	11-20	28
	>20	2
Complication	Without	42
	complication	
	With complication	58

**Table 1**. Characteristics of the Patients with T2DM (n=50) Admitted to the Helvetia Primary Health Centre

By age, 32% of the T2DM patients were in the age range of 56-65 years. The same proportion was also found in the patients aged older than 65 years. More than a quarter (28%) of them were in the age range of 46-55 years. Only 8% of the patients werein the age range of 36-45 years. The T2DM patients had different level of education. Nearly one third (30%) of them graduated from high schools. Twenty eight percent of them only graduated from primary schools. Less than a quarter (22%)of the T2DM patients graduated from junior high schools. Only 20% of them graduated from universities. With regard to occupation, nearly half (48%)of

the patients were housewives. The rest of the T2DM patients were pensionary (20%), enterprisers (18%), officials (8%), and teachers (6%). By duration of the disease, it was found that most of the patients (70%) have suffered from the disease for 0-10 years. Less than one third (28%) of them had suffered from the disease for 10-20 years. Only 2% of them had suffered from the disease for 10-20 years. Only 2% of them had suffered from the disease for more than 20 years. As much as 42% of the patients had no complications and more than half (58%) of them suffered from complications (58%). The utilization of antihyperglycemic drugs in the management of patients with T2DM at the Helvetia health center period June to July 2015 is listed in Table 2.

**Table 2.** Utilization of Antihyperglycemic Drugs in The Management of Patientswith T2DM (n=50)

Drug utilized	Proportion of the patients (%)		
Glibenclamide	44		
Glibenclamide-Metformin	18		
Glimepiride	16		
Metformin	12		
Glimepiride-Metformin	6		
Glimepiride-Glibenclamide	2		
Prodiabet-Metformin	2		

As listed in Table 2, the rank of antihyperglycemic drugs provided to the patients with T2DM in decreasing order were glibenclamide (44%), glibenclamide-metformin (18%), glimepiride (16%), metformin (12%), glimepiride-metformin(6%), glimepiride-glibenclamide (2%), and prodiabet-metformin (2%).

The QOL of the patients with T2DM is demonstrated in Table 3. Overall, mean value of the QOL of the patients with T2DM was  $0.79 \pm 0.14$ . There were only 8 patients had perfect QOL. Five patients had QOL of 0.85. Majority (18) of the patients had the QOL dimensions of 11121 with a score of 0.80. Thus, only 31 (62%) of them had good QOL. Eighteen (36%) of them had fair QOL. One (2%) of the patients had bad QOL.

Number of patients	Mobility	Self care	Daily Activities	Pain	Depression	Score (index value) per patient
8	1	1	1	1	1	1
5	1	1	1	1	2	0.85
18	1	1	1	2	1	0.80
14	1	1	1	2	2	0.73
1	2	1	1	2	2	0.66
1	2	1	2	1	2	0.74
1	2	1	2	2	1	0.69
1	2	1	2	2	2	0.62
1	2	2	2	2	3	0.08

Table 3. The QOL of Patients with T2DM (n=50) Based on the EQ5D

Listed in Table 3 is the association between the age of the patients with T2DM and their QOL. It was proved that the QOL of the patients with T2DM was different in each age level. The

present study found that there was no significant difference between the QOL of males and those of females, p = 0.325. It was also proved that there was no significant association between the age of the patients and their QOL, p = 0.620. In other words, the age of the patients with T2DM did not affect their QOL.

Characteristics		Number of	р			
		Good	Fair	Bad		
Gender	Males	5	11	1	0.325	
	Females	8	25	0		
Age group	36-45	2	2	0	0.620	
	46-55	3	9	1		
	56-65	3	12	0		
	>65	5	13	0		
Education	Primary school	4	10	0	0.377	
	Junior high school	1	10	0		
	Senior high school	5	10	0		
	University	3	6	1		
Occupation	Enterpriser	0	8	1	0.155	
1	Official	1	0	0		
	Teacher	3	3	0		
	Housewife	6	18	0		
	Pensionary	3	7	0		
Duration of	≤10	9	25	0	0.596	
the disease	11-20	4	10	1		
(years)						
× /	>20	0	1	0		
Complication	Without complication	7	14	0	0.446	
	With complication	6	22	1		

Table 4. Association Between the Characteristics and the QOL of the T2DM Patients

The QOL of the patients with T2DM was not associated with their educations, p = 0.377. By occupation, the present study proved that there were no significant differences in QOL among the five groups of patients, p = 0.155. This study also indicated that there were no significant association among the duration of the disease and the QOL of the patients with T2DM, p = 0.596. Result of statistical analysis also proved that there was no significant difference in the average value of the QOL between patients with and without complications, p = 0.446. Complications that may affect the QOL of patients with T2DM include increased blood cholesterol, hypertension, urinary tract infection, cardiovascular disease, nephropathy, retinopathy, and neuropathy.

#### 4. Discussions

The present study found that the age of the T2DM patients was  $59.70 \pm 10.44$  (years). Most of them (66%) were females. This result was not consistent with the sex ratio of the total Indonesian population which is 101.42 males per 100 females of the same year [10]. Additionally, a study proved that females were more prone to develop diabetes because they

have a greater chance to increase body mass index compared to males. Also, monthly premenstrual cycle syndrome and post-menopausal ease the fat accumulate in the body as a result of the hormonal process. These conditions tend to cause higher risk (53.2%) for developing T2DM in females compared to males [11]. A study undertaken in the US also proved that body mass index is a substantial contributor to the increase in the prevalence of diabetes [12]. A large-scale prospective cohort study conducted in Spain also proved that the incidence of T2DM increased with the increasing incidence of obesity [13].

By age, most of the T2DM patients were at the age range of 56-65 years and older. This finding is consistent with the statement of the American Diabetes Association, that people at the age of 45 years or older have a high risk to developT2DM[14]. Aging affects many hormones that regulate metabolism, reproduction and other body functions. Aging affects the pancreatic  $\beta$  cell sensitivity to glucose and delay the mediation of glucose uptake by insulin into the cells[15].

Four of the most frequently provided antihyperglycemic drugs provided to the patients with T2DM with decreasing order were glibenclamide, glibenclamide-metformin, glimepiride and metformin. Glibenclamide is included into sulfonylurea class whose mechanism of action to increase insulin secretion by pancreatic beta cells so as to have a hypoglycemic effect. This drug is an option for adult patients with DM with normal weight who have never experienced ketoacidosis. A previous study conducted in a tertiary care teaching hospital in Eastern India indicated that the most widely used antihyperglycemic agent was biguanide followed by sulfonylureas [16]. Another study proved that the most widely used antihyperglycemic agent was metformin followed by sulfonylurea class of drugs [17]. These studies indicated that the utilization of antihyperglycemic agents vary from one country to another.

The present study found that the index of QOL of patients with T2DM was 0.79. There were limited similar studies conducted in Indonesia. A QOL study conducted on Brunai Malay T2DM patients (n=154) applying EQ5D5L found that the index of their QOL was 0.626 [18]. The QOL of patients with T2DM is an important and measurable outcome of healthcare interventions. It should be considered by policy-makers to prioritize the use of health resources. It was found in this study that the QOL of the patients was not associated with their education. In fact, only 20% of them graduated from universities. This is probably the reason why there was no association between the patients' education and their QOL. The level of education can affect the patients' insight in understanding the disease, self-care and lifestyle settings. In addition, the highly educated patients can easily develop a good understanding of information. These individuals will positively respond the information and take appropriate action for themselves [5]. An ancillary observational analysis of a four-year randomized controlled trial on T2DM patients had greater remission compared with an intensive lifestyle intervention (ILI) with a diabetes support and education control condition (DSE) among 4503 US adults [19].

The duration of the disease by age groups of the patients was not associated with their QOL. In contrast to this study, previous finding indicated that the risk for complications in patients with DM was associated with the duration of the disease. The main risk factors for developing complications in diabetic patients were the duration and severity of the disease. Efforts to improve the QOL are important to prevent from long-term complications [20]. The present study proved that there was no significant association between the age of the patients with T2DM and their QOL.

This study proved that gender was not associated with the QOL of the patients with T2DM. A similar study also confirmed that there was no significant difference in the QOL of males and those of females [21]. Adherence to pharmacological and non pharmacological therapies contributes to improve the QOL of patients with T2DM. Females usually have better adherence to their treatments, thus, the treatment implementation usually goes on better in females compared to males. However, males tend to have higher self confidence and the ability to cope with the disease they suffer. Ultimately, gender was not associated with the level of QOL[21].

It was also proved that occupation, the disease duration, and age groups of the patients were not associated with their QOL. This study also indicated that there was no significant difference in the average value of the QOL between patients with and without complications. In contrast to this study, a finding proved that the complications experienced by the T2DM patients resulted in physical, psychological and even social limitations which ultimately lead to poor QOL[21].

#### 5. Conclusions

Most of the patients with T2DM were females with varies age ranging from 36 years to older than 65 years. Glybenclamide was the most widely provided antihyperglycemic drug to the patients with T2DM. The QOL of the patients was only 79% of full health. The most frequently observed dimensions of 11121 with a score of 0.80. The QOL of the patients was not associated with age, gender, education, occupation, complications as well as the disease duration.

This study was limited by the small sample size and period of the patients' admission from which data were extracted. In the future a large-scale study is required to get more accurate results.

## REFERENCES

- [1] World Health Organization, "Diabetes country profiles", *World Health Organization*, 2016. [Online] Available from: http://www.who.int/diabetes/global-report/en/. [Assessed : Apr. 24, 2017].
- [2] "Diagnosis and Classification of Diabetes Mellitus," *Diabetes Care*, vol. 37, no. Supplement\_1, pp. S81–S90, Dec. 2013.
- [3] J. Lopez, K. Annunziata, R. Bailey, D. E. Morisky, and M. Rupnow, "Impact of hypoglycemia on patients with type 2 diabetes mellitus and their quality of life, work

productivity, and medication adherence," *Patient Preference and Adherence*, p. 683, May 2014

- [4] M. Sutiawati, J. Nurhaedar, Yustini, The influence of diet education on knowledge, eating patterns, and blood glucose level in patients with type 2 diabetes mellitus Lanto'DG Pasewang Jeneponto Hospital", *portalgaruda.org*, August 2013. [Online] Available from: portalgaruda.org/article.php.article-29748&val=2168. [Assessed on Feb. 07 2015]
- [5] D.W. Ningtyas, W. Pudjo, P, Irma, "Analysis of quality of life of patients with type 2 diabetes melitus in Bangil public hospital, district of Pasuruan. Jember", *Repository Unej* 2013. [Online] Available from:http://repository.unej.ac.id/handle/123456789/59225. [Assessed on Feb 10, 2015].
- [6] V. D. Joshi, N. Mooppil, and J. F. Lim, "Validation of the Kidney Disease Quality of Life-Short Form: a cross-sectional study of a dialysis-targeted health measure in Singapore," *BMC Nephrology*, vol. 11, no. 1, Dec. 2010.
- [7] A. Ozder, M.S ekeroglu, H.H. Eker, "Quality of life and satisfaction with treatment in subjects with type 2 diabetes: results from primary health care in Turkey", *Int J Clin Exp Med*, vol. 7, no.12 pp. 5715. 2014
- [8] A. Pichon-Riviere, V. Irazola, A. Beratarrechea, A. Alcaraz, and C. Carrara, "Quality of life in type 2 diabetes mellitus patients requiring insulin treatment in Buenos Aires, Argentina: a cross-sectional study," *International Journal of Health Policy and Management*, vol. 4, no. 7, pp. 475–480, Apr. 2015.
- [9] M.F. Drummond, J.O. Bernie, L.S. Greg, W.T. George, Methods for the Economic Evaluation of Health Care Programs, Second Edition, Oxford University Press, New York, 1997
- [10] World Data Atlas, "Indonesia Population Sex ratio of the total population", World Data Atlas, 2017, [Online]. Available from: https://knoema.com/atlas/Indonesia/topics/Demographics/Population/Sex-ratio. [Assessed on June 22 2017].
- S. Wahyuni, "Factors associated with diabetes mellitus in urban areas in Indonesia 2007", *CORE*, 2010. [Online]. Available from: http://core.ac.uk/pdf/11735485.pdf. [Assessed on 7th October 2015].
- [12] A. Menke, K. F. Rust, J. Fradkin, Y. J. Cheng, and C. C. Cowie, "Associations Between Trends in Race/Ethnicity, Aging, and Body Mass Index With Diabetes Prevalence in the United States," *Annals of Internal Medicine*, vol. 161, no. 5, p. 328, Sep. 2014.
- [13] J. M. Huerta, M.-J. Tormo, M.-D. Chirlaque, D. Gavrila, P. Amiano, L. Arriola, E. Ardanaz, L. Rodríguez, M.-J. Sánchez, M. Mendez, D. Salmerón, A. Barricarte, R. Burgui, M. Dorronsoro, N. Larrañaga, E. Molina-Montes, C. Moreno-Iribas, J. R. Quirós, E. Toledo, N. Travier, C. A. González, and C. Navarro, "Risk of type 2 diabetes according to traditional and emerging anthropometric indices in Spain, a Mediterranean country with high prevalence of obesity: results from a large-scale prospective cohort study," *BMC Endocrine Disorders*, vol. 13, no. 1, Feb. 2013
- [14] "Standards of Medical Care in Diabetes," *Diabetes Care*, vol. 28, no. Supplement 1, pp. S4–S36, Dec. 2004.
- [15] Z. Gong and R. H. Muzumdar, "Corrigendum to 'Pancreatic Function, Type 2 Diabetes, and Metabolism in Aging," *International Journal of Endocrinology*, vol. 2017, pp. 1–2. 2017.
- [16] B. Patel, B. Oza, K. Patel, S. Malhotra, and V. Patel, "Pattern of antidiabetic drugs use in type-2 diabetic patients in a medicine outpatient clinic of a tertiary care teaching hospital," *International Journal of Basic & Clinical Pharmacology*, vol. 2, no. 4, p. 485, 2013.
- [17] S. Mandal, T. Maiti, A. Das, A. Das, A. Mandal, B. Sarkar, and S. Mandal, "Drug utilization study in patients with type 2 diabetes mellitus attending diabetes clinic of a tertiary care hospital in rural Bengal," *International Journal of Basic and Clinical Pharmacology*, pp. 1647–1654. 2016.
- [18] D. Koh, A. M. K. bin Abdullah, P. Wang, N. Lin, and N. Luo, "Validation of Brunei's Malay EQ-5D Questionnaire in Patients with Type 2 Diabetes," *PLOS ONE*, vol. 11, no. 11, p. e0165555, Nov. 2016.

- [19] E. W. Gregg, H. Chen, L. E. Wagenknecht, J. M. Clark, L. M. Delahanty, J. Bantle, H. J. Pownall, K. C. Johnson, M. M. Safford, A. E. Kitabchi, F. X. Pi-Sunyer, R. R. Wing, A. G. Bertoni, and for the Look AHEAD Research Group, "Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes," *JAMA*, vol. 308, no. 23, p. 2489, Dec. 2012.
- [20] S. Rizkifani, D.A. Perwitasari, W. Supadmi, "Measurement of quality of life in patients with diabetes mellitus in PKU Muhammadiyah hospital, Bantul.Yogyakarta", 2014, [Online]. Available from: http://farmasains.uhamka.ac.id/wpcontent/uploads/2015/02/farmasains-uhamka-vol-2-3-Rizkifani-Swww.farmasains.uhamka.ac\_.id\_.pdf. [Assessed on October, 17 2015].
- [21] A.Yusra, "Association between family support and the quality of life in patients `with type 2 diabetes melitus at internal medicine polyclinic in Fatmawati hospital",*Library UI*, 2011, [Online]. Available from: lib.ui.ac.id. [Assessed on Sept 25 2015].