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Article

Development of Multibacillary Leprosy Medication Adherence Evaluation Questionnaire (ML-MAEQ) in Indonesian Patients

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Abstract: Adherence with multidrug therapy (MDT) is one of the keys to successful treatment of leprosy. In order to understand the treatment behavior, reasons for non-adherence, and efforts to improve medication adherence, it is necessary to use a valid and reliable instrument to measure adherence to MDT in multibacillary leprosy patients on regular basis. This study used a mixed method design. The instrument development phase involved 10 experts using 4 rounds of Delphi method. Assessment items that are considered relevant are those that meet 4-5 Likert scale by a minimum of 75% of experts or meet assessment score >3.75 . We did the pilot testing and the questionnaire was revised if invalid. After obtaining a valid and reliable instrument, it was tested to 100 subjects in 4 health centers. For internal validity test, 9 valid assessment items were obtained, with the correlation coefficient values of each item >0.3 , and α -Cronbach's reliability of 0.723. The instrument produced had sensitivity of 88.46% and specificity of 78.37%. From 100 subjects enrolled, 61% had good adherence and 39% had poor adherence based on questionnaire assessment. A valid and reliable questionnaire for evaluating adherence with MDT in Indonesian patients has been composed.

Keywords: adherence; instrument; leprosy; MDT; questionnaire

1. Introduction

Leprosy is a chronic disease which causes very complex problems around the world [1]. Indonesia is the 3rd country with largest number of leprosy cases in the world, after India and Brazil [2]. The prevalence of leprosy in Indonesia in 2021 was 0.45/10,000 with 89% of cases are multibacillary (MB) leprosy [3]. Leprosy requires a long treatment with combination of antibiotics called multidrug therapy (MDT), which has changed the history of leprosy from a disaster to a curable disease [4].

Adherence to treatment is one of the main keys to successful therapy of leprosy [5]. Adherence to treatment is defined as patient behavior in accordance with the advice of health professionals [6,7]. Adherence with MDT in the treatment of leprosy will minimize the risk of relapse, prevent drug resistance, and minimize the risk of leprosy reactions and disabilities [5,8]. The leprosy program routinely uses treatment completion and withdrawal rates as indirect measure of medication adherence. Patients with paucibacillary (PB) leprosy must complete 6 doses of MDT in 6-9 months, whereas the multibacillary (MB) must complete 12 doses in a period of 12-18 months. Patients who do not reach this target are referred to as dropout (defaulter) [5,8]. Defaulter rate which represents the value of medication adherence in leprosy management strategy used so far, actually does not provide any information about treatment behavior and is of little use in preventing irregularity in MDT intake [5].

To understand patient treatment behavior, factors that cause non-adherence to treatment, as well as for the effectiveness of efforts to increase medication adherence, it is necessary to use a tool that is

accurate and practical in measuring medication adherence routinely [9]. A self-reported questionnaire to assess medication adherence is an easy and inexpensive method, brief, comfortable to patients, valid, reliable, and can provide information about treatment behavior and beliefs. This method can also differentiate the type of non-adherence from different causative factors, thus requiring different interventions [9–11]. With the important role of evaluating medication adherence and in effort to overcome the limitations of defaulter rate as parameter of medication adherence to MDT, a valid and reliable measuring tool is needed to assess medication adherence of leprosy patients in daily practice. This research was conducted to answer this need.

2. Materials and Methods

This study used a mixed methods research design, consisted of qualitative and quantitative methods, which will be described as follows.

The Questionnaire Development Stage

a) The questionnaire development stage based on experts panel using Delphi method

We applied the steps of developing instrument using Delphi method based on 10 leprosy experts i.e.: dermatologists who are also lecturers in the field of leprosy, doctors with minimum of 5 years of experience in MDT provider health centers, and the policy maker of leprosy in Indonesia. This stage was also carried out using a seven-step method based on Fowler and Cosenza (2009), Fowler (2014), and Amir (2015)[12–14]. The complete step-by-step description of developing the questionnaire can be seen in the following **Diagram 1**.

b) The questionnaire pre-test stage (pilot testing)

The questionnaire pilot testing was carried out on 10 leprosy patients across 4 health centers (Puskesmas Cakung Jakarta, Fatmawati Hospital Jakarta, dr. Cipto Mangunkusumo National Hospital Jakarta, and dr. Sitanala Leprosy Hospital Tangerang).

The Questionnaire Trial Stage

Cross sectional study design was used to collect data for all variables. The validity test of assessment items (internal validity) was done with Pearson moment products at SPSS 24.0, likewise with the external validity test. The inclusion criteria in this trial stage were: (1) male or female between 17-59 years old, (2) diagnosed with multibacillary type leprosy and were undergoing WHO MDT MB treatment regimen for at least 6 months or release from treatment (RFT) in the last 1 month, (3) were using Indonesian language, (4) could read, (5) had a record during treatment, in the form of medical records or MDT record, including treatment time, (6) brought the last current WHO MDT MB blister regimen which were still being consumed or had been consumed, and (7) willed to become study sample and signed the informed consent. While the exclusion criteria were: (1) patients with MDT drop out, (2) patients who experienced psychiatric disorders in the form of psychosis, anxiety, or depression, and (3) patients with cognitive impairments who were assessed using Mini-Mental State Examination (MMSE) questionnaire. The minimum sample size was obtained by calculating the correlation formula with the r value of 0.3, so it was determined as many as 100 subjects. The assessment item was said to be valid if the p value of the assessment item correlation to the total score <0.05 and the r value >0.3 . Reliability test which measured was the reliability of internal consistency, with α -Cronbach >0.60 .

The formulation of theoretical framework, research objectives and methods

Questionnaire 1 formulation in the form of open-ended questions regarding assessment indicators

Research ethics approval

Send questionnaire 1 in the form of open-ended questions regarding assessment indicators to 10 leprosy experts in Indonesia [Delphi method round 1]

Analyze the answers of questionnaire 1 and then compile them into questionnaire 2 in the form of questions/ statements to assess the relevance of the assessment indicators

Send questionnaire 2 to the 10 leprosy experts (Delphi method round 2)

Analyze the answers of questionnaire 2 (tabulation of assessment items which were given the answer of 'very relevant' by at least 75% of experts) and then compile them into questionnaire 1 pre-test (pilot testing)

Questionnaire pre-test to 10 patients from 4 health centers and then assess its validity and reliability

A valid ($r > 0.3$) and reliable (α -Cronbach > 0.6) questionnaire obtained (n=10)

An invalid ($r < 0.3$) and not reliable (α -Cronbach < 0.6) questionnaire obtained (n=10)

Revision of the questionnaire was then carried out

Send ratings of assessment indicators and final questionnaire proposal. The experts were asked for approval and revision for the final questionnaire proposal, as well as reasons and suggestions if they did not agree (Delphi method round 3)

Test the questionnaire which has been mutually agreed by experts in the sample population (100 subjects in 4 health centers)

If there are any unapproved assessment items or any suggestions for final questionnaire proposal by experts, then revisions are made

Data collection

Data processing, validity and reliability test

A valid and reliable self-reported questionnaire for evaluating medication adherence to MDT in multibacillary leprosy patients

Diagram 1. Research operational framework

3. Results

3.1. The final questionnaire

The final questionnaire (**Table 1**) was the result of assessment items arrangement which had gone through several stages of revision and the third pilot testing with acceptable values of validity and reliability. Researchers used a Likert scale approach. Each assessment item contains 4 answer choices, therefore the researcher determines the lowest score = 1 for poor adherence answer choices, while the highest score = 4 for the good adherence answer choices. We determined a score of 29-36 as the category of good medication adherence, while a score of ≤ 28 as a category of poor medication adherence.

Table 1. Final questionnaire [Multibacillary Leprosy Medication Adherence Evaluation Questionnaire (ML-MAEQ)].

No.	Assessment Items	Never	Sometimes	Often	Always
1	My family helped remind me to take MDT medication.				
2	I take MDT every day according to the instructions on how to take medicines from the health worker.				
3	I showed the MDT drug blister that I had taken to the health worker.				
4	I went to a health facility where I got MDT according to the control schedule.				
5	I missed taking MDT medication because of experiencing drug side effects.				

No.	Assessment Items	Strongly disagree	Disagree	Agree	Strongly agree
6	The long term treatment (12-18 months) made it difficult for me to take MDT medication regularly.				
7	I am sure I can recover by taking MDT medication regularly.				
8	I understand the transmission, reactions, and complications of leprosy, so I take MDT medication regularly.				
9	Family and people around me help support a comfortable situation, so I take MDT medication regularly.				

MDT = multidrug therapy.

3.2. Characteristics of the study samples

Table 2. Sociodemographic characteristics of the study samples (N = 100).

	Characteristics	n (%)	Means \pm SD
Age (years)			
17-30 years old		34 (34.0)	
31-45 years old		38 (38.0)	
46-59 years old		28 (28.0)	
Gender			37.27 \pm 13.45
Male		69 (69.0)	
Female		31 (3.0)	
Marital status			
Single/ never married		41 (41.0)	

Married	57 (57.0)
Divorced/ widowed	2 (2.0)
Level of education	
Never received school education	4 (4.0)
Low education (kindergarten and elementary school)	21 (21.0)
Middle education (junior high school and senior high school)	67 (67.0)
High education (diploma, bachelor, magister, doctoral)	8 (8.0)
Employment	
Employed	60 (60.0)
Unemployed	40 (40.0)

MDT = multidrug therapy ; n = frequency of study samples ; SD = standard deviation.

3.3. Validity and reliability test

The length of time to fill out the questionnaire had time range between 85 to 248 seconds. Internal validity relates to the accuracy degree of the study design with the results achieved[15]. Meanwhile, external validity relates to the generalizability of the study results; whether or not an observed causal relationship can be generalized to and across different measures, persons, settings, and times [16,17]. Pill counts have been used by some investigators as adherence indicators, because they were easy to carry out although have some drawbacks [18]. In this study, pill count was used as criteria to test the external validity of the newly developed questionnaire (**Table 3**). Internal consistency reliability test of the ML-MAEQ gave an α -Cronbach value of 0.723.

Table 3. Results of the internal/ items validity test and the external validity test of medication adherence questionnaire against pill count (N = 100).

No.	Assessment items	Internal Validity		External Validity	
		r	Result	r	Result
1	My family helped remind me to take MDT medication.	0.687	Valid	0.233	Invalid
2	I take MDT every day according to the instructions on how to take medicines from the health worker.	0.594	Valid	0.590	Valid
3	I showed the MDT drug blister that I had taken to the health worker.	0.532	Valid	0.304	Valid
4	I went to a health facility where I got MDT according to the control schedule.	0.483	Valid	0.692	Valid
5	I missed taking MDT medication because of experiencing drug side effects.	0.583	Valid	0.417	Valid
6	The long term treatment (12-18 months) made it difficult for me to take MDT medication regularly.	0.501	Valid	0.096	Invalid
7	I am sure I can recover by taking MDT medication regularly.	0.600	Valid	0.395	Valid
8	I understand the transmission, reactions, and complications of leprosy, so I take MDT medication regularly.	0.615	Valid	0.324	Valid
9	Family and people around me help support a comfortable situation, so I take MDT medication regularly.	0.564	Valid	0.181	Invalid

MDT = multidrug therapy; N = frequency of study samples; r = correlation coefficient.

3.4. Sensitivity and specificity test

Although there has been no gold standard instrument used in measuring MDT adherence until now, the pill count method is considered to be quite favourable and it has been recommended to be used periodically to measure medication adherence [5]. Therefore, in this study the sensitivity and specificity assessment of the new instrument was compared to the pill count (**Table 4**). The analysis

results of ML-MAEQ diagnostic test was found to have a sensitivity value of 88.46%, specificity of 78.37%, positive predictive value (PPV) of 58.97%, and negative predictive value (NPV) of 95.08%.

Table 4. Results of the medication adherence questionnaire score and pill count (N = 100).

		Pill count			
		Result	Poor adherence	Good adherence	Total
Questionnaire		Poor adherence	23	16	39
		Good adherence	3	58	61
		Total	26	74	100

N = frequency of study samples.

4. Discussion

In selecting and using the medication adherence questionnaire, we need to consider of what the scale actually measures and how well it has been validated [10]. As every disease has different characters from one another, no questionnaire is a gold standard for medication adherence measurement [19,20]. According to Ćulig and Leppée, Medication Adherence Questionnaire (MAQ) is the nearest to gold standard test tool, however the internal consistency reliability is not better than some other scales, and it is only capable to identify barriers of medication adherence [10,20,21]. Some of the preexisting medication adherence questionnaires were also likely specific for only certain diseases [10,20,21]. The eight-items Morisky Medication Adherence Scale (MMAS-8) has better validity and reliability than MAQ, but it has good internal consistency and reproducibility only in a few types of diseases [22].

Validity and reliability are the two most important and fundamental features in the evaluation of any instrument [23]. No questionnaire has been tested for its validity and reliability in assessing adherence to MDT. Our study showed that the newly developed instrument or so called the Multibacillary Leprosy Medication Adherence Evaluation Questionnaire (ML-MAEQ) provided good practicality, validity and reliability in Indonesian patients. The causal relationship of one concept to another can be discussed in terms of validity. Internal validity refers to the strength of relationship of a concept to another internal to the research question under study [24]. Internal validity is an essential thing which must be fulfilled if the researchers want the results to be meaningful. It also takes precedence over external validity test, because unbiased results must be reached first before generalization results [25]. From the results of internal validity test, the correlation between each assessment item with the total score was good because all statements had a correlation coefficient >0.3 . Therefore, it can be concluded that each assessment item in ML-MAEQ is worthy of use and accurately assesses what should be assessed.

Internal consistency was used in the questionnaire reliability test. Internal consistency with an α -Cronbach value of 0.6 is considered sufficient for a newly developed scale. The ML-MAEQ gave an α -Cronbach value of 0.723 which indicates this new instrument has a relatively high to good internal consistency [26]. Because there were still no questionnaire been tested for its reliability in assessing medication adherence to MDT, so ML-MAEQ has not comparable to other questionnaires.

External validity is one of the most difficult types of validity to achieve. Many studies face problems when it comes to measure the external validity, to prove the study results can be generalized to a wider population. Most of these studies yield in high internal validity but low external validity[25]. Experts argue that the external validity test results can be invalid if the sample study does not represent the target population [25]. Although this study has been carried out in a multicenter manner, most samples came from health centers which are referral hospitals, which had many experts in dermatology, except for the first line health center Puskesmas Cakung. These health workers were considered to have more skills in evaluating, managing, and providing education about leprosy and MDT. Therefore, the sample obtained in this study was still insufficient to represent the target population, especially those who seek treatment at various first line health centers. Researchers found that although items number 1, 6, and 9 have a weak correlation coefficient, all have positive values. This means that all variables move in the same direction (parallel or linear)

and measure the same manifestations, nothing contradicts. If the observed pattern between two variables is linear, then the correlation coefficient indicates a reliable measure [27]. In order to obtain good validity of an instrument, a large and representative sample size is generally required [28].

Sensitivity shows the probability that the instrument correctly identifies patients who actually suffer from certain disease, while specificity shows how often the instrument is negative in patients who do not have certain disease [29]. ML-MAEQ is worth to be used in screening or evaluating medication adherence to MDT for its good sensitivity and specificity. The PPV indicates how much the result is truly positive when it is found to be positive, while NPV assesses how much an examination result is truly negative when it is found to be negative. These two values have a more profound significance clinical practice for interpretation of results than the sensitivity and specificity [30].

This study had limitations. Although this instrument can be generalized to all multibacillary leprosy patients who got MDT, but some factors including sociodemographic, clinical, and treatment characteristics of this study only described the conditions in Jakarta and Tangerang with patients mainly came from a referral health centres. The same results may not be obtained from multibacillary leprosy patients in other areas, other cultures, private clinics, or in the first line health centres with more subjects proportion than in this study.

5. Conclusions

To the best of our knowledge, this is the first study which produced a valid and reliable instrument for evaluating MDT medication adherence. Further research will determine whether this instrument is valid in other settings, cultures, and borderline type leprosy patients. In addition, to obtain better external validity results, further research should be involving a larger and more varied subject samples (multicentres).

Author Contributions: LSS, SLM and H contributed to the study conception and design. SLM, KB, H and EM contributed to data analysis and supervision. Data collection, analysis, interpretation, and the first draft of the manuscript were predominantly performed by LSS. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Standing Committee for Research Ethics Assessment of Faculty of Medicine Universitas Indonesia, with approval letter number 1089/UN2.F1/ETIK/2018 (October 22nd, 2018) for studies involving humans.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data available on request due to restrictions eg privacy or ethical.

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