The Validity and Reliability of the Indonesian Version of the Chronic Liver Disease Questionnaire (CLDQ) in Measuring Quality of Life in Patients with Liver Cirrhosis

Irsan Hasan[1], Robby Pratomo Putra[2], Evy Yunihastuti[3], Juferdy Kurniawan[1]*

[1] Division of Hepatology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

[2] Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

[3] Division of Allergy and Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Corresponding Author:

Irsan Hasan, MD., PhD. Division of Hepatology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Man gunkusumo Hospital. Jl. Pangeran Diponegoro No. 71, Jakarta 10430, Indonesia. Email: irsan_h@yahoo.com

ABSTRACT

Background: *Liver cirrhosis remains the major cause of liver-related morbidity and mortality around the world. Cirrhosis also negatively affects health-related quality of life. Quality of life evaluation in cirrhosis treatment is often overlooked, despite its importance compared to traditional outcome. One of the specific tools to measure quality of life in cirrhosis patient is the Chronic Liver Disease Questionnaire (CLDQ). Although this tool has been widely used in many countries, no studies have been conducted on its validity and reliability in the Indonesian language. This study aimed to assess the validity and reliability of the Indonesian version of CLDQ using appropriate methods.* ***Methods:*** *This is a cross-sectional study conducted at Hepatobiliary outpatient clinic in Dr. Cipto Mangunkusumo National General Hospital (RSCM), from April-May 2021. The CLDQ was first translated into the Indonesian language and subsequent pretest was performed on 10 people, resulting in the final Indonesian version of the CLDQ. The final version was later tested in the main study with larger number of subjects (52 people). Validity was assessed using construct and external validity tests, while reliability was tested using internal consistency and test-retest methods.* ***Results:*** *The Indonesian version of CLDQ had a good construct validity (r 0.613-0.917), moderate external validity (54.1%), strong correlations between CLDQ and SF-36, good internal consistency (Cronbach-Alpha ≥ 0.7), and good test-retest reliability (ICC > 0.7).* ***Conclusion:*** *The Indonesian version of CLDQ is valid and reliable in measuring the quality of life of liver cirrhosis patients in Indonesia.*

Keywords: *chronic liver disease questionnaire, liver cirrhosis, quality of life, validity, reliability.*

INTRODUCTION

Liver cirrhosis, or frequently simply called cirrhosis, is a disease which remains a major cause of liver-related morbidity and mortality around the world.[1-4] In 2017, cirrhosis caused 1.32 million deaths worldwide (2.4%), a 1.9% increase from 1990 data.[4] Data from the USA showed that cirrhosis ranked 12 in all causes of mortality in 2007.[1] In Indonesia, the epidemiology data of cirrhosis remains lacking. According to one study conducted in a public hospital in Indonesia, the average prevalence of

cirrhosis is 3.5% out of all patients admitted to the Internal Medicine ward.[5]

Liver cirrhosis is irreversible in nature. Therefore, therapies for cirrhosis patients are targeted at palliative aspects instead of curative.[6] The goal of palliative treatment is to increase the quality of life of patients as cirrhosis disrupts the patients' health-related quality of life (HRQoL).[7] The HRQoL terminology resides below the wider quality of life (QoL) terminology, and it is an important multidimensional concept in patient's perspective including physical health, mental health, and social welfare.[8,9] The evaluation of HRQoL in cirrhosis treatment is frequently overlooked, due to the fact that cirrhosis treatment tend to focus only on the clinical aspects or traditional outcome. However, the HRQoL aspects tend to be more important for the patient personally as it pertains to aspects they value, such as the emotional and lifestyle aspects.[10]

There are various generic and specific tools to measure HRQoL in cirrhosis patients. The most widely-used generic tool is short form-36 (SF-36), while the most frequently-used specific tool is the chronic liver disease questionnaire (CLDQ). The CLDQ is widely used in many countries is because it is simple, easy to use, with fewer questions, related closely with severity of chronic liver disease, and it is the first questionnaire which specifically evaluates HRQoL in chronic liver diseases, including cirrhosis.[10,11]

Data about HRQoL in cirrhosis patients in Indonesia is limited, especially data on HRQoL measurements using CLDQ as the evaluation tool. Two studies conducted in two cities in Indonesia (Yogyakarta and Medan) have used CLDQ to evaluate the quality of life in liver cirrhosis patients; however, they have not conducted and reported the validity and reliability of the questionnaire, which raises a question on its translation and adaptation from the original language (English).[12,13] Although the validity and reliability of local versions of CLDQ has already been tested in many countries, the validity and reliability of the native Indonesian version needs to undergo the same testing process, due to the fact that the sociodemographic and clinical characteristics of cirrhosis patients differs from the original CLDQ study.[14] Therefore, this study is conducted to test the validity and reliability of the Indonesian version of CLDQ using appropriate methods according to the questionnaire validation guidelines. The resulting questionnaire could be used to evaluate HRQoL of Indonesian liver cirrhosis patients.

METHODS

This is a cross sectional study conducted in the Hepatobiliary Outpatient Clinic in Dr. Cipto Mangunkusumo National General Hospital (RSCM) from April-May 2021. The study was divided into two periods. The first period was pretest to test the prefinal version of CLDQ that has been translated into the Indonesian language with limited number of subjects (10 people), and the second period was the main research to test thevalidity and reliability of the final Indonesian version of CLDQ with a larger number of subjects (52 people), as determined using sample size formula for correlation tests. The characteristics of subjects in the first period differs from that of the second period. The methods was adapted from a study by Beaton DE, et al.[15] that was also used by several validity and reliability studies. The CLDQ has 29 questions and divided into six domains including: abdominal (AB), fatigue (FA), systemic (SY), activity (AC), emotion (EM), and worry (WO).

Before conducting the pretest, the authors requested permission from the original authors of CLDQ to be translated and validated into Indonesian language. The original English version of CLDQ was then translated and adapted with the help of four certified and experienced translators. Two Indonesian speaker translators (one with medical background and one with none) were assigned for the forward translation (English to Indonesian) and the other two were English speaker translators who were assigned for the backward translation (Indonesian to English). Every time the translator finished, the authors analyzed, synthesized, and discussed the translation results with all of the translators. After forward translation is completed, the pre-final Indonesian version of CLDQ was generated and pre-tested to 10 respondents who

matched the inclusion and exclusion criteria. The respondents' feedback from pre-test were included and the questionnaire was subsequently backward translated, resulting in the final Indonesian version CLDQ final version. The final version was assessed for its validity and reliability on 52 respondents, who also fulfilled the pre-determined criteria. Questionnaires were distributed using consecutive sampling methods. The validity of the Indonesian version of CLDQ was assessed using the construct and external validity tests, while its reliability was assessed using internal consistency and test-retest approach. The study flowchart is presented in the **Figure 1**.

Data were processed and analyzed using statistical package for social sciences (SPSS) for Windows version 21.0. Construct validity was analyzed using multitrait- multimethod analysis approach, and external validity was analyzed by conducting correlation test between CLDQ and other questionnaire. In this study, the SF-36 as a generic questionnaire was used due to several reasons: SF-36 is widely used in other validity and reliability studies in the other countries, it is the only questionnaire that has been translated and validated in Indonesian language to measure the quality of life in liver cirrhosis, and there are no other specific questionnaire besides CLDQ that has been translated and validated in Indonesian language. Internal consistency was assessed using Cronbach- Alpha coefficient and test-retest approach was used to calculate intraclass correlation coefficient with one-week interval.

Ethics

Ethical approval for this study was obtained from the Medical Research Ethics Committee of the Faculty of Medicine Universitas Indonesia, Dr. Cipto Mangunkusumo National Central General Hospital number: KET- 134/UN2. F1/ETIK/PPM.00.02/2021. All subjects were provided detailed information about the study, and have signed the informed consent form voluntarily. All subjects' information was kept confidential.

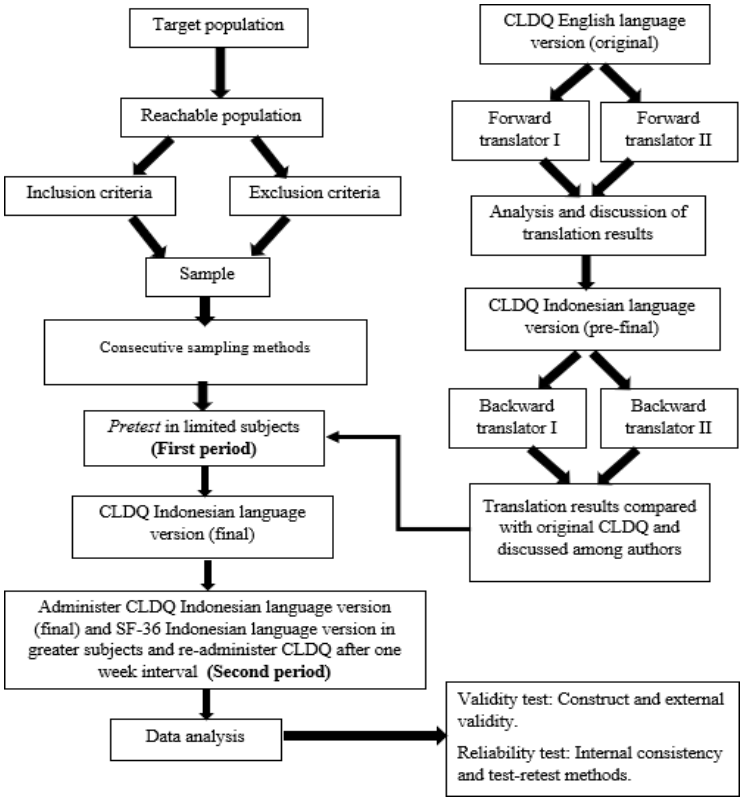

Figure 1. Study flowchart.

RESULTS

Fifty-two subjects were recruited from the Hepatobiliary Outpatient Clinic in Cipto Mangunkusumo Hospital (CMH) from April-May 2021, to test the final Indonesian version of CLDQ. **Table 1** shows the subjects' characteristics.

Table 1. Characteristics of study subjects.

Variables	N=52
Gender, n (%)	
Male	37 (71.2)
Female	15 (28.8)
Age, average (SD)	53 (SD 10.18)
Marital status, n (%)	
Married	45 (86.5)
Single	2 (3.8)
Divorced/widow/widower	5 (9.6)
Educational background	
Elementary school	9 (17.3)
Middle school (junior and senior high)	30 (57.7)
University	13 (25.0)
Ethnicity, n (%)	
Javanese	23 (44.2)
Sundanese	6 (11.53)
Batavia	8 (15.38)
Padang	5 (9.61)
Bataknese	10 (19.23)
Occupation, n (%)	
Unemployed	21 (40.38)
Private sector employee	12 (23.07)
Public sector employee	4 (7.69)
Others	13 (25)
Income per month, n (%)	
< Rp 5,000,000.00	44 (84.61)
Rp 5,000,000.00-Rp 10,000,000.00	6 (11.53)
> Rp 10,000,000.00	2 (3.84)
Time since diagnosis of cirrhosis, n (%)	
<5 years	38 (73.1)
5-10 years	11 (21.2)
>10 years	3 (5.8)
Child-Pugh score, n (%)	
A	33 (63.5)
B	16 (30.8)
C	3 (5.8)
History or current ascites,	
Yes	9 (17.3)
No	43 (82.7)
History of hepatic encephalopathy	
Yes	0 (0.0)
No	52 (100.0)
History of esophageal varices ligation	
Yes	25 (48.07)
No	27 (51.92)
Hepatitis B or C serological marker	
HBsAg (-), Anti-HCV (-)	3 (5.8)
HBsAg (-), Anti-HCV (+)	19 (36.5)
HBsAg (+), Anti-HCV (-)	29 (55.8)
HBsAg (+), Anti-HCV (+)	1 (19)

The first result of the study was the translation and adaptation process of the CLDQ. The first translation, which was a forward translation from English to Indonesian language, did not produce any significant problems. Although there were discrepancies in some questions of the questionnaire between the two forward translators, such as bodily pain translated into *nyeri pada bagian tubuh* by the first translator, and *nyeri pada tubuh* by the second translator, the authors managed to synthesize, analyze, and discuss with both of the translators and chose the best words, phrases, grammars, and sentences that truly represent the meaning of the questions being asked without compromising the practicality and effectiveness of the sentences. This is done in order to prevent confusion of the subjects.

The similar finding was also found in the backward translation. After the backward translators gave the authors their translation results, the authors synthesize, analyze, and compared them with the original English language of CLDQ. There were no significant differences between both of the translation results and the original CLDQ, although there were slight differences in some word choices, but not compromising the meaning of the original questions. The backward translators are not familiar with (blinded) the original language of CLDQ.

The prefinal CLDQ version was produced after the aforementioned process, and small amount of subjects could fill in the questionnaire without significant difficulties. There were no subjects confused with the questions being asked in the questionnaire. The average time of the subjects filled in the questionnaire was relatively short, which was 5.3 minutes. The process of filling in the prefinal CLDQ version was termed the pretest process, and the results was considered to make the final CLDQ version that was used in larger amount of subjects to test for validity and reliability.

The main results of the study were the validity and reliability of the final Indonesian version of CLDQ. The questionnaire's construct validity was assessed using multitrait-multimethod analysis, with good validity defined as good correlation between scores of each CLDQ questions with their own domains, which is also known as convergent validity. On the other hand, items with good construct validity must also have weaker correlation with other domains they do not belong to, known as discriminant validity. Good correlation is defined as having r 0.3-0.6 (moderate) and r > 0.6 (strong), while r < 0.3 is defined as weak correlation. Our analysis found that 93.1% of all CLDQ questions showed strong correlations (r > 0.6) with their own domains and 6.9% had moderate correlations (r 0.3-0.6), while most of the questions had weaker correlations with other domains. **Table 2** shows the construct validity CLDQ.

The external validity of the questionnaire was tested using Spearman correlation test between CLDQ (six domains) and SF-36 (eight domains). Our analysis found that there were 54.1% good correlations (8.3% strong correlations with r 0.6-0.79 and 45.8% moderate correlations with r 04-0.59). The rest of the correlations were found to be weak and very weak. **Table 3** shows the external validity of the questionnaire.

To test for the reliability of the questionnaire, internal consistency was assessed by measuring Cronbach-Alpha in each of the CLDQ domains and the overall questionnaire, with the good internal consistency defined as having Cronbach-Alpha ≥ 0.7. The test-retest method on the other hand, was tested by having respondents complete

Table 2. Construct validity of CLDQ in Indonesian language

	CLDQ Domains					
CLDQ Question Numbers	**AB**	**FA**	**SY**	**AC**	**EM**	**WO**
1	**0,877***	0,449	0,522	0,543	0,484	0,375
5	**0,898***	0,449	0,522	0,543	0,484	0,375
17	**0,917***	0,551	0,485	0,658	0,576	0,431
2	0,579	**0,769***	0,454	0,529	0,553	0,362
4	0,329	**0,774***	0,388	0,387	0,438	0,406
8	0,499	**0,848***	0,479	0,501	0,543	0,448
11	0,520	**0,848***	0,470	0,558	0,618	0,504
13	0,285	**0,688***	0,430	0,375	0,236	0,228
3	0,729	0,507	**0,613***	0,577	0,522	0,231
6	0,305	0,294	**0,615***	0,463	0,374	0,090
21	0,302	0,299	**0,695***	0,353	0,386	0,246
23	0,267	0,352	**0,659***	0,213	0,340	0,438
27	0,149	0,317	**0,554***	0,232	0,227	0,176
7	0,570	0,489	0,533	**0,846***	0,461	0,415
9	0,568	0,630	0,463	**0,857***	0,513	0,264
14	0,604	0,417	0,508	**0,850***	0,588	0,338
10	0,410	0,566	0,571	0,399	**0,817***	0,620
12	0,508	0,495	0,501	0,700	**0,789***	0,600
15	0,377	0,496	0,332	0,515	**0,593***	0,459
16	0,473	0,323	0,415	0,461	**0,719***	0,345
19	0,557	0,640	0,563	0,494	**0,864***	0,733
20	0,552	0,380	0,431	0,501	**0,751***	0,382
24	0,362	0,333	0,565	0,470	**0,626***	0,419
26	0,309	0,495	0,453	0,376	**0,741***	0,471
18	0,300	0,410	0,344	0,308	0,568	**0,850***
22	0,345	0,484	0,344	0,265	0,569	**0,874***
25	0,304	0,429	0,351	0,395	0,619	**0,852***
28	0,483	0,459	0,343	0,365	0,590	**0,788***
29	0,353	0,323	0,334	0,349	0,461	**0,644***

*Bolded numbers have p < 0.05, with all numbers in the table being r value (correlation). Abbreviations: CLDQ: chronic liver disease questionnaire, AB: abdominal, FA: fatigue, SY: systemic, AC: activity, EM: emotion, WO: worry.

Table 3. External validity of CLDQ in Indonesian language.

	SF-36							
Domains	**PF**	**MH**	**EV**	**SF**	**RLP**	**RLE**	**BP**	**GH**
CLDQ:								
AB	0,344*	0,630*	**0,544***	0,099	0,343*	0,446*	0,564*	0,487*
FA	0,490*	0,487*	**0,583**	0,187	0,440*	**0,509***	0,270	0,180
SY	**0,515***	0,340*	0,401*	0,032	0,366*	0,503*	0,298*	0,092
AC	0,461*	0,539*	**0,505***	0,162	0,509*	**0,520***	0,387*	0,332*
EM	0,395*	0,682*	**0,645***	0,381*	0,431*	**0,611***	0,304*	0,306*
WO	0,507*	0,526*	**0,406***	0,185	0,303*	0,457*	0,108	0,398*

*Numbers with asterisks have $p < 0.05$ and bolded numbers have moderate (r 0.4-0.59) and strong (r 0.6-0.79) correlations. All numbers in the table represents r value (correlation). Abbreviations: CLDQ: chronic liver disease questionnaire, AB: abdominal, FA: fatigue, SY: systemic, AC: activity, EM: emotion, WO: worry, SF-36: short form- 36, PF: physical functioning, MH: mental health, EV: energy/vitality, SF: social functioning, RLP: role limitation due to physical health, RLE: role limitation due to emotional problem, BP: bodily pain, GH: general health.

the questionnaire two times with a one week interval. The correlation between the test and retest scores was measured using intraclass correlation coefficient (ICC) between domains scores and overall questionnaire scores. The analysis showed that the Cronbach- Alpha of all the domains in the Indonesian version of CLDQ and overall CLDQ were good, with $\alpha \geq 0.7$. The ICC of all domains and overall questionnaire also has good and very good correlation (good and very good correlation are defined as having ICC of 0.61-0.8 and > 0.8, respectively). Table 4 below presents the reliability test result for the questionnaire.

DISCUSSION

The subjects of this study showed some similarities in characteristics with subjects in the other validity and reliability studies, such as the majority gender in this study being men (71.2%) which is similar with studies in Thailand (63.5%), China (75.4%), India (85.2%), Singapore (68.2%), Germany (53%), Greece (65%), Italy (63.9%), Persia (64.5%), Serbia (54.4%), and Spain (70.5%).[16-25] The average age of the subjects in this study was 53 ± 10.18 years old which does not differ significantly from studies in Thailand (51.6 ± 8.9 years), Germany (52.7 ± 13.9 years), Serbia (53.8 ± 12.9 years), and Spain (55.25 ± 12.83 years).[16,20,24,25] Subjects in this study were mostly married (86.5%) and this is similar to studies in Thailand (81.3%), China (86.9%), and Singapore (85.5%).[15,16,18] The educational background in this study was dominated by middle school graduates (57.7%), which is similar to studies in Singapore (59.1%) and China (64%). It is important to note that the subjects educational background provided no hindrance towards understanding the CLDQ questions because the sentences are simple and easy to understand.[16,18] Other sociodemographic characteristics do not have similarities with other countries, such as: ethnicity, unemployment status, and low income defined as less than Rp 5,000,000.00 per month.

Table 4. Reliability of CLDQ in Indonesian language

CLDQ Domains	Cronbach-Alpha	ICC (95% CI)
Abdominal (AB)	0.927	0.864 (0.774-0.919)
Fatigue (FA)	0.861	0.757 (0.611-0.853)
Systemic (SY)	0.884	0.793 (0.665-0.876)
Activity (AC)	0.858	0.752 (0.604-0.850)
Emotion (EM)	0.937	0.881 (0.802-0.930)
Worry (WO)	0.909	0.834 (0.727-0.901)
Overall CLDQ	0.947	0.900 (0.832-0.941)

As for the clinical characteristics of the subjects, the majority of subjects in this study had been diagnosed with liver cirrhosis for less than 5 years (73.1%), with Child- Pugh A stage (63.5%). The majority also did not have ascites (82.7%), nor had they experienced hepatic encephalopathy (100%). The results are similar with studies in Thailand, Singapore, and Greece, which conducted their sampling in the outpatient clinic, therefore making the clinical characteristics of the patients similar. The

majority of patients had stable and compensated liver cirrhosis profiles.[16,19,21] In terms of history of esophageal varices ligation, there was no significant difference between respondents, which could be seen in every stage of cirrhosis, although was commonly found from Child-Pugh B cirrhosis. Most of the respondents in this study (55.8%) had positive HBsAg serological marker without positive anti-HCV, and this is similar with other studies in Singapore (78.9%) and Greece (44.5%). This is likely due to the high prevalence of Hepatitis B infection in Indonesia, Singapore, and Greece.[19,21]

The construct validity of the questionnaire showed that all of the CLDQ questions had moderate and strong correlations with their own domains (6.9% and 93.1% had moderate (r 0.3-0.6) and strong (r > 0.6) correlations, respectively), indicating a good convergent validity. The majority of the CLDQ questions also had weaker correlations with other domains they do not belong to, indicating that the questionnaire had good discriminant validity. The results of the current study demonstrated better validity with an r ranging from 0.554-09.917, than a study from Singapore, with r of 0.43-0.84.[19] The difference might be due to difference in subjects recruited for the validity test, where the study from Singapore recruited all chronic liver disease patients and not just patients with cirrhosis, in contrast to the only-cirrhosis patients recruited in this study. With good convergent and discriminant validity, it could be concluded that the Indonesian version of CLDQ has good construct validity.

The second validity testing method was the external validity. Our analysis revealed that there were 54.1% moderate and strong correlations between the CLDQ and the SF-36 domains, while the rest of the correlations were weak and very weak. This result differs from that of two studies from Singapore and India, with 66.6% moderate correlations and no strong correlation in the Singaporean study, and 70.8% moderate correlations and 20.8% strong correlations in the Indian study.[18,19] The difference might be due to different types of HRQoL measurement between CLDQ and SF-36. CLDQ domains are more specific to measure the HRQoL in liver cirrhosis patients than SF-36 domains which are more generic. Consequently, there were questions with no correlations between the CLDQ and SF-36 domains. For example, the AB domain in CLDQ focuses more on problems related to the abdominal area, and did correlate with the SF domain in SF-36, which focuses more on the social functions disrupted by the disease, such as: activity with friends, family, or society. However, the number of moderate and strong correlations in the Indonesian version of CLDQ remains above 50%, indicating a good external validity. With good construct and external validity, it can be concluded that the Indonesian CLDQ is valid for measuring the health-related quality of life in Indonesian patients with liver cirrhosis.

For reliability testing, the current study used internal consistency and test-retest methods. The Cronbach-Alpha in all of CLDQ domains were in the range of 0.858-0.937, while overall Cronbach-Alpha was 0.947. The Cronbach-Alpha in this study is similar with studies from Thailand (0.93-0.94), Greece (0.74-0.94), Japan (0.809-0.971), and Sweden (0.75-0.96).[16,21,26,27] The fact that this study revealed a good Cronbach-Alpha (>0.7) indicates that the Indonesian version CLDQ has a good internal consistency, meaning that there was a good correlation between one CLDQ questions and the other.

The test-retest method analysis with Spearman correlation found that the ICC of the Indonesian version of CLDQ was in the range of 0.752-0.864, and the overall ICC was 0.9. The results were similar with studies in Germany (0.78-0.86), India (0.74-0.92), Spain (0.727-0.903), and Sweden (0.73-0.88).[18,20,25,27] However, this study used a different interval of retest with the other studies: one week compared to 3-8 days in Germany, two weeks in India, Spain, and Sweden. The reason this study used one week as an interval for retest was because in one week it is expected that no significant changes has occurred in the subjects that could affect the study results, and not too short that the subjects may still remember their own answers. With a good ICC of more than 0.7, the Indonesian CLDQ has good test-retest results, indicating a good correlation between the same domain and overall CLDQ scores in the first day (test) and the eighth day

(retest). The fact that the internal consistency and test-retest reliability is good, indicates that that the Indonesian version of CLDQ is reliable in measuring the health-related quality of life in Indonesian patients with liver cirrhosis.

The strength of this study lies in the fact that it revealed good validity and reliability of the Indonesian version of the CLDQ in measuring the quality of life of Indonesian liver cirrhosis patients. The study has followed the established questionnaire validation guidelines used by other validity and reliability studies. This study is also the first in Indonesia to conduct a validity and reliability test towards specific HRQoL questionnaire in liver cirrhosis patients. The limitation of this study is the feasibility problem of the CLDQ question number 29 when it is applied in Indonesian population. The question asks about the perception of patients regarding the liver availability for transplant. Although all subjects could answer the question without any problem and understood the question very well, the availability of liver donor remains low in Indonesia. This explains the low rate of liver transplant in our country.

CONCLUSION

The Indonesian version of CLDQ has good validity and reliability and can be used to measure the quality of life in liver cirrhosis patients in Indonesia.

AUTHOR CONTRIBUTION

All authors contributed equally in this study from idea and study design, data collection, data analysis, and article writing and revision.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in this study.

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