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ORIGINAL RESEARCH

Cost-effectiveness of albumin in the treatment of decompensated cirrhosis in resource-limited healthcare settings

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Abstract

Background: Human albumin (HA) is an effective adjuvant treatment for patients with cirrhosis developing spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS) and ascites requiring large-volume paracentesis (LVP). However, cost remains a barrier to use, particularly in resource-limited settings. This study aims to assess the cost-effectiveness of HA in patients with cirrhosis with SBP, HRS or ascites requiring LVP in the Indonesian healthcare system as a representative of a resource-limited setting.

Methods: Three decision-tree models were developed to assess the cost-effectiveness of (1) antibiotics and HA *versus* antibiotics alone in patients with SBP, (2) terlipressin and HA *versus* terlipressin alone in patients with HRS, and (3) LVP and HA *versus* LVP and gelatine for patients with ascites. Clinical utility and economic inputs were pooled from the available literature. Time horizon was 3 months. Outcomes were expressed as incremental cost-effectiveness ratios (ICER) reported as 2021 IDR per quality-adjusted life year (QALY) (exchange rate June 30, 2021: 1 EUR = 17,245 IDR). Willingness-to-pay thresholds considered were: three times the GDP per capita (199,355,561 IDR/QALY; 11,560 EUR/QALY) and one time the GDP per capita (66,451,854 IDR/QALY; 3853 EUR/QALY).

Results: The ICER for antibiotics and HA (*versus* antibiotics alone) for SBP was 80,562,652 IDR per QALY gained (4672 EUR/QALY). The ICER for terlipressin and HA (*versus* terlipressin) for HRS was 23,085,004 IDR per QALY gained (1339 EUR/QALY). The ICER for LVP and HA *versus* LVP and gelatine was 24,569,827 IDR per QALY gained (1425 EUR/QALY).

Conclusion: Adjunctive HA may be a cost-effective treatment for SBP, HRS and LVP in resource-limited settings.

Keywords: cost-effectiveness, human albumin, Indonesia, liver cirrhosis, liver diseases, resource-limited settings.

Citation

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Key points for decision-makers

- Clinical guidelines for the treatment of complications related to cirrhosis, namely spontaneous bacterial peritonitis, hepatorenal syndrome and ascites requiring large-volume paracentesis, recommend the addition of human albumin infusion to improve recovery and reduce complications.
- Cost of human albumin limits its use in resource-limited settings.
- This study, using three decision-tree models, assessed the cost-effectiveness of albumin for the treatment of cirrhosis complications in Indonesia as a model of a resource-limited healthcare setting.
- The findings emphasize that the additional benefit gained from using human albumin in treating cirrhosis complications is worth the additional cost.

Background

Liver cirrhosis represents an advanced stage of chronic liver disease characterized by irreversible liver damage.[1] Liver cirrhosis poses a significant global health concern, contributing substantially to liver-related morbidity and mortality.[2–5] Decompensated cirrhosis, an advanced and severe clinical condition, is associated with numerous life-threatening complications, including ascites, variceal gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome (HRS) and severe jaundice.[6] These complications occur at an annual rate of 5–7%,[7] leading to frequent hospitalizations and imposing a significant economic burden.

Human albumin (HA) is widely used for the treatment of decompensated cirrhosis, particularly in addressing complications such as HRS, spontaneous bacterial peritonitis (SBP) and ascites requiring large-volume paracentesis (LVP) (>5 L). Its efficacy in these conditions has been well established and is recommended in international guidelines.[8–10] Randomized clinical trials and meta-analyses have demonstrated the efficacy of HA to treat and prevent clinical complications of cirrhosis, which are characterized by effective hypovolaemia.[8–12] Recently, HA has emerged as a potential disease-modifying agent in decompensated cirrhosis. In addition to its oncotic properties, HA exhibits non-oncotic actions that target various aspects of the disease, including effective hypovolaemia, endothelial inflammation, oxidative stress and drug metabolism.[11] It is worth noting that the effects of HA can be influenced by factors such as the timing of infusion, specific indications, infusion strategy, baseline serum albumin level and severity of cirrhosis.[8–12]

Despite recommendations to use HA, its cost remains a barrier to its effective utilization in many countries with resource constraints. However, it is essential to consider the economic burden associated with cirrhosis complications and subsequent healthcare costs, including frequent hospitalizations and prolonged treatment periods.

The high incidence of liver diseases attributed to viral and metabolic factors has been raised as a notable concern in the Asia-Pacific region, including Indonesia, leading to a high prevalence of cirrhosis. Moreover, the limited availability of liver transplantation as a curative intervention intensifies the challenges associated with managing this condition, requiring greater emphasis on palliative care and effective management of complications associated with decompensated cirrhosis.[2,13,14]

Considering the high burden associated with cirrhosis and the budgetary constraints, cost-effectiveness analyses may help guide healthcare decision-making, balancing clinical and socio-economic concerns. In this context, the aim of this analysis is to evaluate the cost-effectiveness of HA in the treatment of acute complications of decompensated cirrhosis, with a specific focus on resource-limited healthcare settings. The current analysis is from the perspective of the Indonesian National Healthcare System. The decision tree models originally developed by Runken et al.[15] for three European countries were confirmed to be applicable by a panel of Indonesian hepatologists and updated with data inputs specific to Indonesia.

Methods

General methods

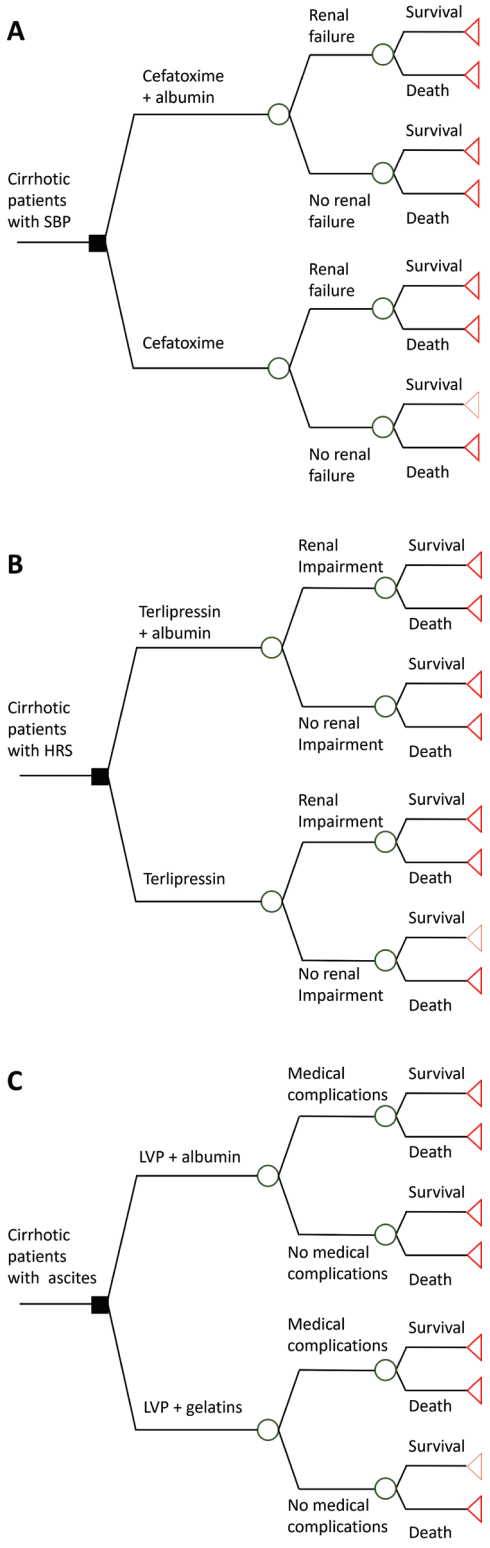
In order to assess the cost-effectiveness of HA for the treatment of SBP, HRS and ascites requiring LVP in a resource-limited country, the decision-tree economic models developed by Runken et al.[15] were populated with Indonesian inputs to consider the perspective of the Indonesian National Healthcare System (Figure 1).

Following the same methods as the original model,[15] the decision-tree models use a 3-month time horizon that is in line with the follow-up time of trials assessing HA use in the three indications of interest.[16–18] The appropriateness of the model, time horizon and data inputs were assessed via a survey to seven hepatologists from the Indonesian Association for the Study of the Liver. Answers to the survey were confirmed and discrepancies were discussed and resolved during subsequent meetings with hepatologist medical advisors (all of whom are authors or listed in the acknowledgements).

All costs were transformed to 2021 IDR based on the inflation rate of the country, and no discount rate was applied (exchange rate on June 30th, 2021: 1 EUR = 17,245 IDR). The output of the decision-tree cost-effectiveness models were incremental cost-effectiveness ratios (ICER) per quality-adjusted life year (QALY). The specific interventions and clinical, economic, and quality of life inputs considered for each indication are specified in the corresponding sub-sections of the methods for each indication (SBP, HRS and LVP).

In order to estimate the QALY, the mortality rates associated with each of the interventions were gathered from clinical trials and multiplied by the utilities for patients with each specific complication following the methods from the model developed by Runken et al.[15] The specific clinical and utility inputs applied for each intervention are specified in the methods subsection for each indication.

Figure 1. Structure of the decision-tree models developed for (A) spontaneous bacterial (SBP), (B) hepatorenal syndrome (HRS) and (C) large-volume paracentesis (LVP). *Medical complications include hyponatraemia, renal impairment and hepatic encephalopathy.



*Medical complications include: hyponatraemia; renal impairment and hepatic encephalopathy.
HRS: hepatorenal syndrome; LVP: Large-volume paracentesis; SBP: spontaneous bacterial peritonitis.

In order to determine whether the interventions evaluated herein were cost-effective, two different willingness-to-pay thresholds were considered: three times the GDP per capita (199,355,561 IDR/QALY [11,560 EUR/QALY]) and a more conservative scenario considering one time the GDP per capita (66,451,854 IDR/QALY [3853 EUR/QALY]) based on the Health Technology Assessment Guideline by the Indonesian Health Technology Assessment Committee.[19]

To assess the uncertainty of the model and robustness of the ICER calculated herein, a probabilistic sensitivity analysis was performed. For all three decision-tree models, clinical, economic and utility inputs were sampled for 1000 simulations, and the probabilities of HA being cost-effective based on the two willingness-to-pay thresholds considered for the three indications were estimated. The list of inputs, standard errors and distributions used in the probabilistic sensitivity analyses are listed in Supplementary Tables S1–S3 (available at: https://www.drugsincontext.com/wp-content/uploads/2024/04/dic.2024-1-1-SupplTables.pdf).

Methods for each of the three indications studied (SBP, HRS and LVP) are presented in the following corresponding sub-sections. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist is available at: https://www.drugsincontext.com/wp-content/uploads/2024/04/dic.2024-1-1-Suppl.pdf).

Spontaneous bacterial peritonitis

The target population for this economic evaluation was patients with decompensated cirrhosis hospitalized due to the development of SBP. Following recommendations from current clinical guidelines,[8–12] the therapeutic strategies assessed consisted of antibiotics and HA *versus* antibiotics alone (Figure 1A).

Clinical inputs (i.e. rates of renal impairment, length of hospital stay and mortality) were gathered from a

Table 1. Clinical inputs and references considered in the decision-tree model for spontaneous bacterial peritonitis based on treatment.

Parameter	Treatment		
	Antibiotics + albumin	Antibiotics alone	References
Renal impairment incidence (%)	9%	31%	18,20,21
Hospital length of stay (days)	14	13	18
Mortality (%)	17%	37%	18,20,21

literature review including all randomized clinical trials that assessed the effectiveness of antibiotics and HA compared with antibiotics alone[18,20,21] (Table 1). In line with the original model developed by Runken et al.[15] and the definitions included in the original clinical trials, renal impairment was defined as non-reversible deterioration of renal function during hospitalization.[15,18]

Economic inputs included the cost of the pharmacological treatment (cefotaxime and HA). The total dose of antibiotics (cefotaxime, 8 g/day for 5 days) and HA (1.5 g/kg up to a maximum of 100 g on day 1, followed by 1 g/kg on day 3) was based on the current guideline recommendations.[9–11] The average patient weight was assumed to be 65 kg for men and 55 kg for women, assuming a 2:1 male-to-female distribution of patients with cirrhosis based on Indonesian data from the Global Burden of Disease Study 2019.[22] Based on an average patient weight of 62 kg, a total dose of 155 g of HA was assumed.

Other economic inputs included in the model consisted of the average cost for a hospitalization day and the cost associated with the renal impairment complication (Table 2).

QALY for patients with SBP was calculated based on mortality rates gathered from all randomized clinical trials available and utility values reported by Afiatin et al. for Indonesian patients developing sepsis (0.31).[23]

A probalistic sensitivity analysis following the methods detailed in the General methods section was performed. The specific inputs, standard errors and distributions applied are listed in Supplementary Table S1.

Hepatorenal syndrome

The target population for this cost-effectiveness model was patients with decompensated cirrhosis hospitalized with HRS. Treatment strategies considered were terlipressin and HA *versus* terlipressin alone as first-line therapy based on the current clinical guideline recommendations[9–12] (Figure 1B).

Clinical inputs considered in the model were renal impairment and mortality. Rates and utility values were gathered from a literature review that identified one non-randomized study comparing terlipressin and HA *versus* terlipressin alone in patients with cirrhosis and HRS[17] (Table 3). It was assumed that patients who did not achieve a complete (decrease in serum creatinine to ≤1.5 mg/dL) or partial (50% decrease in serum creatinine to >1.5 mg/dL) response had renal impairment.[15,17] In line with the model originally developed by Runken et al.[15] and the clinical evidence considered in this model,

Table 2. Unit costs and references considered in the decision-tree models.

Cost input	Cost 2021 IDR (2021 EUR)	Assumption	References
Pharmacological treatments			
Albumin (g)	47,673 IDR (2.76 EUR)	Average cost of all available presentations has been considered	19,33
Cefotaxime (g)	5182 IDR (0.30 EUR)		
Terlipressin (mg)	485,000 IDR (28.12 EUR)		
Gelatine (100 mL)	26,366 IDR (1.53 EUR)	Gelatine polysuccinate (Gelafusal, Dexa Group, Jakarta, Indonesia) 4% has been considered	
Complications			
Renal impairment	17,130,183 IDR (993,34 EUR)	Average cost per patient based on a retrospective analysis, including patients with 582 kidney disease from 6 hospitals in Indonesia, including class A, B and private hospitals	34
Hospitalization day	1,190,013 IDR (69.01 EUR)	Total cost and average length of stay for patients with Child–Pugh C cirrhosis has been considered	35
Hyponatraemia	4,776,470 IDR (276.98 EUR)	Average cost for in-hospital admission due to cirrhosis has been considered (less severe: B-4-10-I, mild: B-4-10-II and severe: B-4-10-III)	36
Hepatic encephalopathy	12,852,144 IDR (745.27 EUR)	10.8 days average length of hospitalization due to cirrhosis complications and 1,190,013 IDR average cost per hospital have been considered	35,37

Table 3. Clinical inputs and references considered in the decision-tree model for hepatorenal syndrome based on treatment.

Parameter	Terlipressin + albumin	Terlipressin alone	References
Renal impairment incidence (%)	23.1%	75.0%	17
Mortality (%)	46.2%	87.5%	17

patients who did not achieve a complete or partial response were assumed to have renal impairment. The rate of renal impairment was calculated as 1 minus the percentage of patients with improved renal function.[15,17]

Economic inputs included the cost of renal impairment and the pharmacological treatments (terlipressin and HA). The total dose of HA was 235 g assuming 1 g/kg on day 1 and 20–40 g/day after that until reversal of HRS or a maximum of 15 days and a total of 44 mg of terlipressin (1 mg every 4–6 h, increased to a maximum of 2 mg every 4–6 h) for the combination group, and 34 mg of terlipressin alone (Table 2).

QALY for patients with HRS was calculated based on mortality rates and utility values for decompensated cirrhosis reported by Walker et al.[24] (0.75) following the methods described in the General methods section.

A probalistic sensitivity analysis following the methods detailed in the General methods section was performed. The specific inputs, standard errors and distributions applied are listed in Supplementary Table S2.

Large-volume paracentesis

The target population for this economic evaluation was patients with decompensated cirrhosis and ascites requiring greater than 5 L of ascitic fluid removal. On the basis of expert opinion and consensus of the authors on the available literature,[25,26] treatment strategies considered were LVP and HA *versus* LVP and gelatine as the most common plasma expanders used following LVP in Indonesia (Figure 1C).

Clinical inputs were gathered from a literature review that included all randomized clinical trials comparing LVP with HA *versus* LVP with gelatine.[27–29] Clinical inputs considered in the model include the rate of hyponatraemia, hepatic encephalopathy, renal impairment and mortality pooled from all three trials comparing LVP with HA *versus* LVP with gelatine[27–29] (Table 4). In line with the model originally developed by Runken et al.[15] and with the clinical trials included in the model, renal impairment was defined as an increase in the serum creatinine concentration of more than 50% from the pretreatment value to a level greater than 133 µmol/L (1.5 mg/dL).[15,27]

Table 4. Clinical inputs and references considered in the decision-tree model for large-volume paracentesis based on treatment.

Treatment	Albumin	Gelatine	References
Hyponatraemia incidence (%)	14.9%	21.3%	27–29
Renal impairment incidence (%)	7.8%	11.6%	27–29
Hepatic encephalopathy incidence (%)	7.8%	9.8%	27–29
Mortality (%)	4.5%	7.3%	27–29

Economic inputs included pharmacological treatment (HA and gelatine). Based on the dosing recommended in current clinical guidelines, the model used 8 g of HA per 1 L of ascitic fluid removed by LVP for the HA arm and 150 mL of gelatine per 1 L of ascitic fluid removed by LVP for the gelatine arm. In addition, based on expert opinion and standard clinical practice in Indonesia, LVP was assumed to be 5 L on average; therefore, 40 g of HA and 750 mL of gelatine per LVP were assumed. Other economic inputs considered in the model were costs associated to the following clinical complications: hyponatraemia, hepatic encephalopathy and renal impairment (Table 2).

QALY for patients undergoing LVP was calculated based on mortality rates and utility values for decompensated cirrhosis reported by Walker et al.[24] (0.75). An additional disutility of 0.19 was applied to those patients developing hepatic encephalopathy based on the original cost-effectiveness model by Runken et al.[15]

A probalistic sensitivity analysis following the methods detailed in the General methods section was performed. The specific inputs, standard errors and distributions applied are listed in Supplementary Table S3.

Results

Results for each of the three indications studied (SBP, HRS and LVP) are presented in the following corresponding sub-sections.

Spontaneous bacterial peritonitis

The total cost per patient with SBP treated with antibiotics and HA was 4,845,783 IDR (281 EUR) higher than that for patients treated with antibiotics alone (25,794,062 IDR *versus* 20,948,279 IDR; 1496 EUR *versus* 1215 EUR). However, the addition of HA was associated with a reduction in the development of renal impairment and mortality, leading to a gain of 0.06 QALY (0.257 *versus* 0.197) (Table 1 and Figure 2). Overall, the ICER for antibiotics and HA was 80,562,652 IDR per QALY gained (4672 EUR/QALY) compared with antibiotics alone, which is below the willingness-to-pay threshold of three times the GDP per capita 199,355,561 IDR/QALY (11,590 EUR) but above the threshold considering one time the GDP per capita 66,451,854 IDR/QALY (3853 EUR/QALY). Therefore, adding HA to antibiotics would likely be a cost-effective intervention for patients with SBP in Indonesia.

The probabilistic sensitivity analysis showed that the addition of HA to antibiotics had a probability of 99.6% of being cost-effective at a willingness-to-pay threshold of three times the GDP per capita (199,355,561 IDR/QALY (11,560 EUR/QALY)) and a probability of 37.1% of being cost-effective at a willingness-to-pay threshold of one time the GDP per capita (66,451,854 IDR/QALY (3853 EUR/QALY)) (Figure 3A). The parameters included in the sensitivity analysis are detailed in Supplementary Table S1.

Hepatorenal syndrome

The addition of HA to terlipressin for the treatment of patients with cirrhosis developing HRS led to a cost increase of 7,158,571 IDR (415 EUR) compared with that of patients treated with terlipressin alone (36,496,208 IDR *versus* 29,337,638 IDR; 2116 EUR *versus* 1701 EUR). Adding HA to terlipressin also led to increased survival and a reduction in the rate of renal impairment, which led to an incremental

Figure 2. Total and incremental cost (A), and total and incremental QALY for the different interventions assessed for each target population (B). QALY, quality-adjusted life year; LVP, large-volume paracentesis.

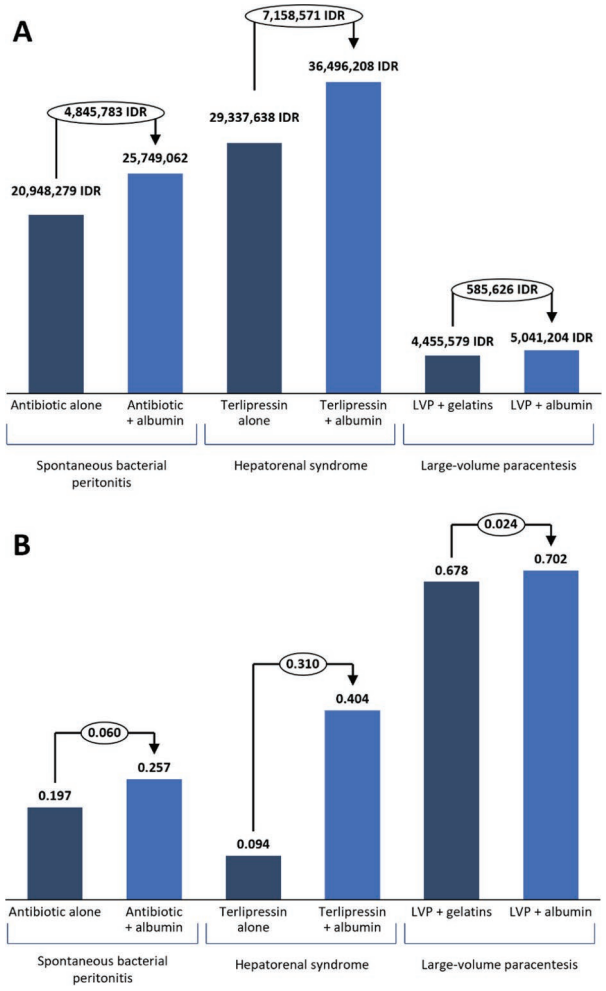
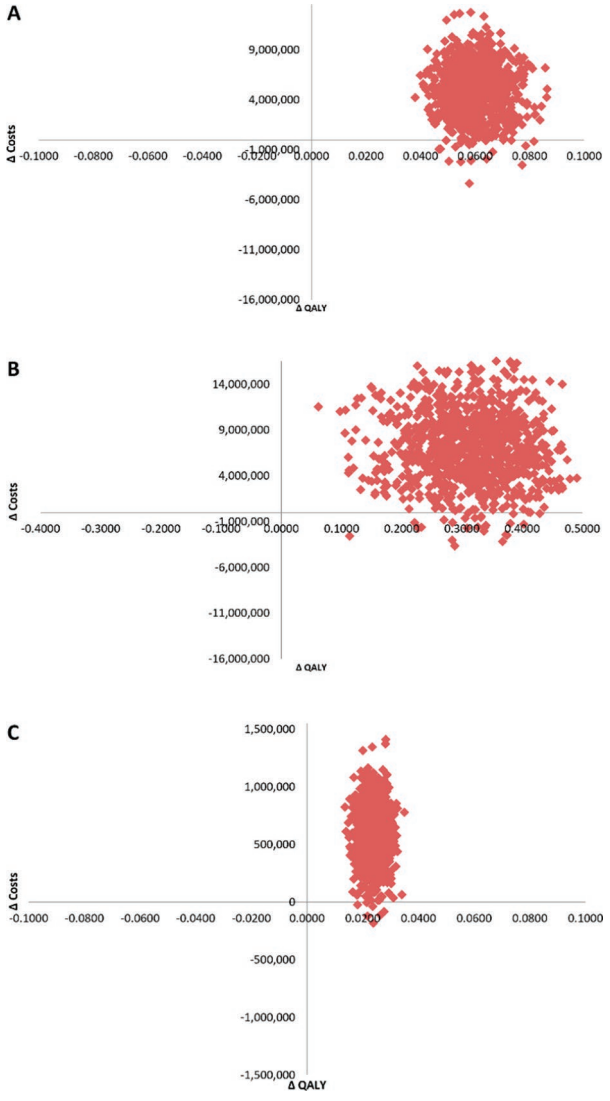


Figure 3. Result of the simulation probabilistic analysis for the cost per quality-adjusted life year (QALY) for (A) spontaneous bacterial, (B) hepatorenal syndrome and (C) large-volume paracentesis.



QALY of 0.310 (0.404 *versus* 0.094) (Table 3 and Figure 2). As a result, the ICER for terlipressin and HA *versus* terlipressin alone was 23,085,004 IDR per QALY gained (1339 EUR/QALY). This ICER is below both willingness-to-pay thresholds considered for health economics evaluations in Indonesia; therefore, HA and terlipressin would be cost-effective compared with terlipressin alone in Indonesian patients with cirrhosis developing HRS.

Based on the probabilistic sensitivity analysis, terlipressin and HA would have a 99.7% and a 98.0% probability of being cost-effective at a willingness-to-pay of three times the GDP per capita (199,355,561 IDR/QALY (11,560 EUR/QALY)) and one time the GDP per capita (66,451,854 IDR/QALY (3853 EUR/QALY)), respectively, compared with terlipressin alone (Figure 3B). The parameters included in the sensitivity analysis are detailed in Supplementary Table S2.

Large-volume paracentesis

The cost per patient undergoing an LVP with HA was 585,626 IDR (33.9 EUR) greater than with gelatine (5,041,204 IDR *versus* 4,455,579 IDR; 292 EUR *versus* 258 EUR). However, LVP with gelatine was associated with an increased risk of hyponatraemia, renal impairment, hepatic encephalopathy and mortality compared with LVP and HA, which overall led to a QALY increase of 0.024 for LVP and HA (*versus* LVP and gelatine) (0.702 *versus* 0.678) (Table 4 and Figure 2). Therefore, the ICER for LVP and HA *versus* LVP and gelatine was 24,569,827 IDR per QALY gained (1425 EUR/QALY), which would be below both willingness-to-pay thresholds considered; therefore, LVP with HA would be considered a cost-effective intervention compared with LVP with gelatine for patients with cirrhosis and ascites in Indonesia.

The probabilistic sensitivity analysis showed that LVP and HA would have a 99.7% and a 100% probability of being cost-effective at a willingness-to-pay of one time the GDP per capita (66,451,854 IDR/QALY (3853 EUR/QALY)) and three times the GDP per capita (199,355,561 IDR/QALY (11,560 EUR/QALY)), respectively, compared with LVP and gelatine (Figure 3C). The parameters included in the sensitivity analysis are detailed in Supplementary Table S3.

Discussion

In this study, the cost-effectiveness of HA as an adjunctive treatment for SBP, HRS and LVP in a resource-constrained country was assessed by modifying the decision-tree economic models developed by Runken et al.[15] to the Indonesian National Healthcare System perspective. This analysis demonstrates that the use of HA, in combination with the recommended treatments, may be a cost-effective intervention for the management of these three conditions in countries with limited healthcare resources like Indonesia. In addition, the findings of this study are consistent with previous research evaluating the use of HA in SBP, HRS and LVP.[15]

In the context of SBP, intravenous HA administration in addition to antibiotics has been demonstrated to delay renal function decline and lower mortality compared with antibiotics alone.[18,20,21] HA administration has also been shown to decrease mortality, avoid complications, improve the management of ascites, and reduce hospitalizations, improving the treatment of patients with cirrhosis developing SBP both clinically and from a healthcare resource utilization perspective.[30] Additionally, preliminary results from a retrospective database analysis showed that infusion of HA in addition to antibiotics within the first 24 hours of hospital admission was associated with a significant decrease in overall inpatient costs for patients with cirrhosis who were admitted with SBP.[31] Overall, these results seem to indicate that the additional cost of HA is counterbalanced by a reduction in healthcare resource utilization and support the clinical guidelines recommendation to use a combination of antibiotics and HA as a first line of treatment for patients with cirrhosis developing SBP.[8–12,32] Such improved effectiveness and reduced healthcare resource utilization reported in previous studies is in line with the findings of the present study. The ICER for antibiotics and HA *versus* antibiotics alone is below the willingness-to-pay threshold of three times the GDP per capita for health economics evaluations in Indonesia, further strengthening the rationale for adopting this treatment approach as standard of care in clinical practice in resource-limited countries.

The use of terlipressin and HA for the treatment of HRS has been shown to improve survival and reduce the rate of renal impairment compared with terlipressin alone.[17] Furthermore, the ICER estimated herein for this combination was below both willingness-to-pay thresholds considered in Indonesia, indicating that it is a cost-effective intervention for patients with HRS in resource-limited countries. This finding aligns with current clinical guideline recommendations to combine terlipressin and HA to manage HRS.[8–12]

With regards to HA use in patients undergoing LVP, patients with cirrhosis presenting with tense ascites undergoing LVP without appropriate plasma expansion are at risk of paracentesis circulatory dysfunction. Several randomized clinical trials and meta-analyses have shown that HA lowers the risk of paracentesis circulatory dysfunction in individuals with cirrhosis presenting with tense ascites and requiring LVP,[16,27,28] thereby placing HA as the optimal plasma expander to avoid this severe

complication. The present cost-effectiveness analysis showed that HA was a cost-effective intervention compared with gelatine for patients with decompensated cirrhosis and ascites requiring at least 5 L of ascitic fluid removal, which is consistent with the original model developed by Runken et al. in three European countries.[15]

The probabilistic sensitivity analyses conducted in this study further support the robustness of ICERs calculated for each of the three indications, with high probabilities of HA being cost-effective in most scenarios considered. This further reinforces that HA is cost-effective when considering the overall cost of treatment, reduction of mortality, reduction of liver-related complications and improvement in quality of life. Therefore, adherence to international clinical guidelines is recommended to optimize the utilization of HA.[8–12] However, in countries facing financial constraints, the use of HA is often restricted by hospital administrations and health authorities due to its higher cost compared with other fluids, leading to an underutilization of HA for indications supported by strong clinical evidence such as SBP, HRS and LVP.[10]

It is worth noting that the current study has some limitations. First, the decision-tree models used in this analysis were based on a 3-month time horizon because the three indications explored herein are acute conditions; therefore, the models are not intended to capture the long-term costs and benefits of HA. Additionally, the study relies on available clinical evidence that may not reflect real-world clinical practice in resource-constrained countries such as Indonesia. In this context, alternative dosing regimens (to that used in available clinical evidence) that could impact both the cost and effectiveness of the treatment were not explored. Additionally, some potential sub-group analysis assessing the cost-effectiveness of HA in patients at a higher risk of developing complications could not be performed due to lack of clinical evidence with such level of granularity. However, these limitations are mitigated by the use of local cost and utility data (when available), and through the validation of all inputs with a panel of experts in the management of patients with decompensated cirrhosis in Indonesia. Indonesia was selected as a model for a resource-constrained country but the clinical practices and costs for each country may vary.

Conclusion

In conclusion, the present study demonstrates that the use of HA as an adjunctive treatment for SBP, HRS and LVP is cost-effective in a resource-constrained environment. These findings place HA as a valuable therapeutic option, emphasizing the importance of incorporating both clinical and cost-effectiveness criteria into healthcare decision-making to optimize outcomes and improve the management of patients with decompensated cirrhosis in resource-limited settings.

Contributions: EV contributed to the model conceptualization and design, literature review, model programming, data acquisition and interpretation, and drafting and approval of the manuscript. DK and CHZ contributed to the literature review, data interpretation and drafting of the manuscript. IH, ISM, PB and KFK contributed to the literature review, data validation, data interpretation, and drafting of the manuscript. ISM also contributed to data acquisition. All authors critically reviewed the manuscript and approved the final version and its submission to *Drugs in Context*. All authors are accountable for the integrity of the work. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Availability of data and materials: All relevant data are contained within the results. Input data were derived from the listed references.

Disclosure and potential conflicts of interest: IH and ISM have served on an advisory board for Grifols and received support for attending meetings. PB has served on an advisory board for Grifols. IH has also received speaker fees from Grifols. CHZ is an employee of Grifols Asia Pacific. DK is an employee of IQVIA on contract to Grifols Asia Pacific. EV is an employee of Grifols SA. KFK received support for attending meetings. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: https://www.drugsincontext.com/wp-content/uploads/2024/03/dic.2024-1-1-COI.pdf

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