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Evaluation of the efficacy, safety and economy of different amphotericin B formulations in invasive fungal disease: A retrospective cohort study

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ABSTRACT

Background: Fungal infections have emerged as an increasingly serious public health challenge globally. Four Formulations of amphotericin B are widely used in antifungal therapy. Despite the same active ingredient, they probably differ in efficacy, safety and economics.

Aim: This study aimed to explore the differences in efficacy, safety and economy among different formulations of amphotericin B in patients with IFD.

Methods: We conducted a retrospective study at a tertiary hospital, examining patients who were administered amphotericin B from June 2023 to March 2025, to assess the efficacy, safety and economy of different amphotericin B Formulations in invasive fungal disease.

Results: (1) A total of 71 patients were included. Patients with potential renal injury are more likely to choose liposomal amphotericin B ($p = 0.021$). (2) Liposomal amphotericin has the accelerated therapeutic onset ($p = 0.042$), amphotericin B deoxycholate has the delayed therapeutic effect ($p = 0.031$), the effective response of liposomal amphotericin B in elders was significantly lower ($p = 0.022$), and the counterpart of amphotericin B deoxycholate in females was significantly higher ($p = 0.01$). (3) The main adverse events of the three amphotericin B formulations were kidney injury ($p < 0.001$), there was no significant inter-group difference. (4) The amphotericin B deoxycholate group incurred the most economical total cost ($p < 0.01$), daily cost ($p < 0.01$) and cost-effectiveness.

Conclusion: Amphotericin B formulations exhibit marked variations in efficacy and economy profiles, necessitating individualized selection guided by specific clinical characteristics. Rigorous monitoring of renal function remains imperative throughout the therapeutic course.

Introduction

Invasive fungal disease (IFD) has become an increasingly serious public health challenge worldwide. Over 2.1 million people develop invasive *aspergillosis* in the context of chronic obstructive pulmonary disease, intensive care, lung cancer, or haematological malignancy, with a crude annual mortality of 1.8 million (85.2 %) annually. About 1.6 million people experience a *Candida* bloodstream infection or invasive *candidiasis* each year, with more than 0.99 million deaths (63.6 %).[1] As a well-characterized polyene agent, amphotericin B remains a cornerstone of antifungal therapeutics.[2] Its mechanism of action primarily involves specific binding to ergosterol in fungal cell membranes, resulting in disruption of membrane integrity and permeability. This broad-spectrum antifungal agent exhibits significant clinical efficacy against various invasive fungal infections, particularly those attributable to *Candida* and *Cryptococcus species*. The American Society of Infectious Diseases (IDSA) has recommended amphotericin B deoxycholate as the initial treatment choice for invasive candidiasis in newborns.[3]

Four distinct formulations of amphotericin B have been developed to date: amphotericin B deoxycholate (AMB-D), liposomal amphotericin B (L-AMB), amphotericin B colloidal dispersion (ABCD), and amphotericin B lipid complex (ABLC). Despite the same active ingredient, they differ in

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pharmacological characteristics such as structure, shape, size, composition, and toxicity.[4] AmB-D displays particular lipoprotein binding affinity, preferentially associating with high-density (HDL) and low-density lipoproteins (LDL).[5] Pharmacokinetic studies reveal that 20–40 % of administered AmB-D undergoes renal and fecal elimination within one week, with urinary concentrations exceeding those of other formulations.[6] The larger molecular configurations of ABLC and ABCD facilitate rapid sequestration by mononuclear phagocyte system components, leading to significant hepatosplenic accumulation while maintaining relatively low plasma concentrations.[5] Notably, ABLC demonstrates enhanced pulmonary tissue penetration.[6] In contrast, compact particle size and anionic surface charge minimize phagocytic clearance of L-AmB, resulting in superior plasma pharmacokinetics and enhanced Central Nervous System (CNS) biodistribution relative to alternative formulations.[7] These pharmacological properties could contribute to variations in therapeutic efficacy and safety profiles. Jadhav MP et al. demonstrated that L-AmB appears to be equally efficacious and safer than AMB-D in febrile neutropenia.[8] Diego R Falci et al. documented that the nephrotoxicity associated with AMB-D is significantly higher compared to L-AMB and ABLC.[9] Conversely, a pharmacovigilance analysis by Yuka Nokura et al., utilizing the FDA Adverse Event Reporting System (FAERS), found no statistically significant disparity in renal or hepatic adverse event frequencies between L-AMB and AMB-D.[10]

Invasive fungal disease (IFD) exhibits heterogeneous clinical manifestations from diverse infection site distributions. Furthermore, IFD progression may induce systemic inflammatory response syndrome (SIRS), culminating in compromised renal perfusion through impaired microcirculatory dynamics. These pathophysiological complexities necessitate rational selection of amphotericin B formulations as a critical therapeutic consideration. This investigation employs real-world statistic to evaluate efficacy, safety and economy among various amphotericin B preparations in IFD management, providing evidence-based clinical decision-making on antifungal regimen optimization.

Methods

Date collection

This retrospective observational study was conducted in a tertiary hospital in China from June 2023 to March 2025. Inclusion criteria: (I) Patients aged 18 years or above ; (II) Patients with IFD and received any formulation of amphotericin B for treatment. IFD is diagnosed according to the criteria established by the European Organization for Research and Treatment of Cancer and the Mycology Study Group (EORTC/MSG).[11] Exclusion Criteria: Patients with incomplete, inaccurate, or missing data were excluded from the study.

The following demographic and clinical data were extracted from the hospital information system (HIS): age, gender, IFD diagnosis, pathogen test, underlying diseases, length of hospital stay, Amphotericin B regimen and other concomitant drugs, adverse drug reactions (ADRs) and biochemical indicators [Blood platelet (PLT), White blood cell (WBC), Neutrophil (%), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Total bilirubin (TBIL), C-reactive protein (CRP), Procalcitonin (PCT), Serum creatinine (SrCr), Creatinine clearance rate, Serum potassium].

Outcome definitions

Therapeutic efficacy was assessed through longitudinal monitoring of clinical parameters and defined using standardized criteria: (I) Complete response: resolution of all clinical manifestations with normalization of laboratory parameters and radiographic findings, accompanied by negative fungal cultures; (II) Partial response: measurable improvement in clinical manifestations and diagnostic markers without complete resolution, irrespective of fungal culture status; (III) Ineffective response: absence of clinical improvement or disease progression evidenced by deteriorating laboratory/imaging parameters, including cases with persistent positive and death cultures. Both patients with complete response and partial response are regarded as effective response.

For the safety evaluation, renal injury was diagnosed and graded according to KDIGO guidelines. Liver injury are characterized by an elevation of aspartate transaminase or alanine transaminase to more than twice the upper limit of normal, or an elevation of total bilirubin to more than twice the upper limit of normal. Hypokalemia indicates that the potassium concentration is lower than 3.5 mmol/L.[12] Thrombocytopenia is defined as a platelet count $< 100 \times 10^9$/L or a 25 % decrease from baseline. Infusion-related reactions include fever, chills, nausea, vomiting. When evaluating adverse drug reactions, patients with corresponding underlying diseases were excluded.

In the economic evaluation, the total cost is defined as the cumulative expenditure for using any formulation of amphotericin B; the daily cost is the ratio of the total cost to the total number of days of using the formulation; and the cost/effectiveness is the ratio of the total cost to the effective response rate achieved by using the formulation.

Statistical analysis. This retrospective observational cohort study categorized patients into three groups based on the amphotericin B formulation administered. The primary outcome was the effective response rate for invasive fungal infections. Based on prior literature, the anticipated response rates for the AMB-D, L-AMB, and ABCD groups were 38 %, 52 %, and 85.8 %[13–15], respectively. With a two-sided α of 0.05 and 80 % power, a total sample size of 59 patients was determined using PASS 15.

Categorical variables were described by numbers and percentages. The continuous variables of normal distribution were described by the mean and standard deviation (SD), and the non-normal distribution data were described by median and interquartile range (IQR). Categorical variables were compared using the chi-square test or Fisher's exact test as needed. For the continuous variables, we applied the ANOVA test to validate the difference between the means in the groups of interest. Kaplan-Meier (KM) curves and the Log-rank test were employed to assess the effective response and adverse events among the different amphotericin B formulations. When $p < 0.05$, the result was considered statistically significant. All statistical analyses were performed in SPSS v22 and Microsoft office Excel 2021, graphical representations were generated in Graph Pad Prism 9.5.

Results

Demographic and clinical characteristics

The retrospective cohort analysis included 71 patients stratified into three cohorts according to amphotericin B formulation (Table 1). The study population demonstrated a median age of 64 years (70.4 % male), with balanced demographic characteristics across cohorts. Comorbidity profiles revealed renal disorders (59.2 %) as the most prevalent underlying condition, followed by hepatic impairment (49.3 %) and diabetes mellitus (40.8 %). Specially, patients receiving L-AMB demonstrated significantly higher proportions of baseline renal disorders and proven etiological diagnoses ($p = 0.021$, 0.034). *Aspergillus species* (32.4 %) and *Mucorales* (9.9 %) emerged as the predominant causative agents, with additional isolates including *Rhizopus* and *Candida species* et al. Pathogen distribution varied across cohorts, with the L-AMB cohort exhibiting a significantly higher prevalence of *Aspergillus* infections ($p = 0.022$). Regarding the distribution of fungal detection sites, sputum was the most common site, accounting for 42.3 % of all detections, followed by urine (12.7 %) and blood (9.9 %). There was no significant difference in the detection sites among the three groups. Simultaneously, the AMB-D cohort exhibited superior creatinine

Table 1
Demographic and clinical characteristics of patients.

	Patients (n = 71)	AMB-D (n = 20)	L-AMB (n = 20)	ABCD (n = 31)	*p*
Age (years)	64.0 (54.0, 71.0)	66.0 (56.8, 72.8)	58.5 ± 14.5	65.0 (56.0, 71.0)	0.245
Gender (male)	50.0 (70.4 %)	14.0 (70.0 %)	12.0 (60.0 %)	24.0 (77.4 %)	0.412
Underlying diseases					
Hypertension	24.0 (33.8 %)	7.0 (35.0 %)	5.0 (25.0 %)	12.0 (38.7 %)	0.595
Diabetes	29.0 (40.8 %)	9.0 (45.0 %)	9.0 (45.0 %)	11.0 (35.5 %)	0.721
Hepatic disorders	35.0 (49.3 %)	7.0 (35.0 %)	10.0 (50.0 %)	18.0 (58.1 %)	0.274
Renal disorders	42.0 (59.2 %)	10.0 (50.0 %)	17.0 (85.0 %)	15.0 (48.4 %)	**0.021***
Malignant tumor	15.0 (21.1 %)	7.0 (35.0 %)	4.0 (20.0 %)	4.0 (12.9 %)	0.167
immunodeficiency disease	19.0 (26.8 %)	5.0 (25.0 %)	4.0 (20.0 %)	10.0 (32.3 %)	0.614
Previous kidney diseases	7.0 (9.9 %)	4.0 (20.0 %)	2.0 (10.0 %)	1.0 (3.2 %)	0.146
Previous dialysis	3.0 (4.2 %)	1.0 (5.0 %)	1.0 (5.0 %)	1.0 (3.2 %)	0.934
Diagnostic certainty					
Proven	36.0 (50.7 %)	9.0 (45.0 %)	15.0 (75.0 %)	12.0 (38.7 %)	**0.034***
Probable	9.0 (12.7 %)	2.0 (10.0 %)	2.0 (10.0 %)	5.0 (16.1 %)	0.744
Possible	26.0 (36.6 %)	9.0 (45.0 %)	3.0 (15.0 %)	14.0 (45.2 %)	0.061
Infectious bacteria					
Aspergillus	23.0 (32.4 %)	3.0 (15.0 %)	11.0 (55.0 %)	9.0 (29.0 %)	**0.022***
Mucor	7.0 (9.9 %)	1.0 (5.0 %)	3.0 (15.0 %)	3.0 (9.7 %)	0.569
Others[21]	26.0 (36.6 %)	9.0 (45.0 %)	10.0 (50.0 %)	7.0 (22.6 %)	0.092
Detection site					
Sputum	30.0 (42.3 %)	8.0 (40.0 %)	11.0 (55.0 %)	11.0 (35.5 %)	0.376
Blood	7.0 (9.9 %)	4.0 (20.0 %)	2.0 (10.0 %)	1.0 (3.2 %)	0.146
Urine	9.0 (12.7 %)	5.0 (25.0 %)	3.0 (15.0 %)	1.0 (3.2 %)	0.069
Length of hospital stay	19.0 (11.0, 28.0)	20.0 (13.3, 35.8)	19.0 (11.0, 27.2)	19.0 (12.0, 27.0)	0.161
Length of amphotericin B	7.0 (4.0, 12.4)	6.60 (4.0, 12.0)	5.9 (3.0, 9.8)	9.0 (4.0, 14.5)	0.413
Concomitant medication					
β-Lactams	63.0 (88.7 %)	19.0 (95.0 %)	17.0 (85.0 %)	27.0 (87.1 %)	0.563
Triazoles	35.0 (49.3 %)	10.0 (50.0 %)	10.0 (50.0 %)	15.0 (48.4 %)	0.991
Glycopeptides	15.0 (21.1 %)	8.0 (40.0 %)	5.0 (25.0 %)	8.0 (25.8 %)	0.483
Diuretics	33.0 (46.5 %)	11.0 (55.0 %)	9.0 (45.0 %)	13.0 (41.9 %)	0.651
Laboratory examination					
PLT (10^9/L)	130.0 (52.0, 242.0)	167.5 ± 133.3	131.9 ± 104.8	115.0 (56.0, 268.0)	0.512
WBC (10^9/L)	7.0 (3.3, 12.6)	6.8 (2.1, 12.4)	6.7 (3.4, 12.4)	7.2 (3.6, 13.4)	0.318
Neutrophil (%)	61.8 (77.4, 85.4)	69.8 (22.7, 84.9)	81.5 (65.7, 85.6)	77.8 (70.6, 85.7)	0.254
CRP(mg/L)	66.8 (26.0, 149.0)	46.4 (28.3, 103.9)	114.9 ± 101.0	74.02 (18.2157.7)	0.522
PCT (ng/mL)	0.5 (0.2, 3.6)	0.2 (0.2, 3.6)	1.4 (0.2, 11.6)	0.6 (0.2, 2.2)	0.572
Creatinine clearance rate	94.0 (51.9 , 129.3)	124.1 ± 73.9	87.9 ± 43.2	81.3 ± 40.7	**0.046***
Creatinine	67.9 (51.5 , 88.6)	58 (42.9, 77.9)	83.4 (59.3, 132.8)	64 (52.2, 81.0)	**0.043***
ALT	20.5 (9.0, 38.7)	18.9 (11.0, 25.9)	22.4 (9.7, 60.7)	16.3 (8.9, 44.6)	0.578
AST	24.2 (14.6, 37.7)	19.7 (14.8, 43.2)	24.8 (15.8, 67.8)	25.4 (13.8, 35.3)	0.591
Total bilirubin	10.6 (8.6, 23.1)	10.5 (7.5, 14.1)	12.6 (7.6, 27.1)	12.3 (9.4, 24.6)	0.197
Potassium	3.9 ± 0.6	4.2 ± 0.5	3.7 ± 0.6	3.8 ± 0.7	0.155

WBC：white blood cell；CRP：C-reactive protein；PCT：Procalcitonin; ALT: alanine aminotransferase; AST, aspartate aminotransferase; *P*: Compare the differences among AMB-D, L-AMB and ABCD cohorts. *: there was statistical difference between the cohorts; the baseline is set as the last examination before the first administration of the drug.

clearance rates (124.1 vs 87.9 vs 81.3 mL/min, $p = 0.046$) compared to the other two cohorts, with correspondingly lower serum creatinine levels (58.0 vs 83.4 vs 64.0 mg/dL, $p = 0.043$).

Comparison of efficacy

The cohort demonstrated overall response rates of 26.8 % complete response (19/71), 38.0 % partial response (27/71), and 35.2 % ineffective response (25/71). Comparative analysis revealed formulation-specific response patterns (Fig. 1): AMB-D showed the superlative effective response (complete/partial response, 70.0 %), while L-AMB was associated with the greatest ineffective response(45.0 %). There were no significant differences among the three cohorts ($p > 0.05$).

We conducted a stratified analysis of patients based on age, gender, underlying comorbidities, and diagnostic certainty **(**Table 2**)**. Specifically, the effective response rate of L-AMB in elderly patients was significantly lower (71.4 % vs 22.2 % vs 73.7 %, $p = 0.022$) compared to the other formulations, and the counterpart of AMB-D in female patients was significantly higher (100.0 % vs 25.0 % vs 28.6 %, $p = 0.01$), Furthermore, ABCD exhibited significantly enhanced efficacy in cases with possible diagnoses (77.8 % vs 50.0 vs 100.0 %, $p = 0.023$). Simultaneously, As depicted in Fig. 3**,** L-AMB achieved significantly higher response rates within 3 days compared to other formulations in both effective response ($p = 0.042$) and complete response cohorts ($p = 0.026$). Conversely, AMB-D demonstrated superior after 7 days response rates in the effective response cohort ($p = 0.031$). However, the Kaplan-Meier survival curve indicates no significant difference in the time to effective response among the three groups (Fig. 2).

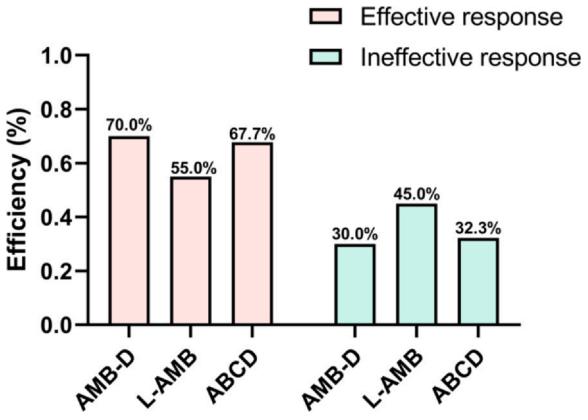

Fig. 1. Therapeutic response between different amphotericin B formulations.

Table 2
Therapeutic response of different amphotericin B.

	AMB-D	L-AMB	ABCD	*p*
age (years)				
19–40	1/1 (100.0 %)	2 /3(66.7 %)	1/3 (33.0 %)	0.459
41–60	3 /5(60.0 %)	7/8 (87.5 %)	6/9 (66.7 %)	0.483
61–83	10/14 (71.4 %)	2/9 (22.2 %)	14/19 (73.7 %)	**0.022***
gender				
male	8/14 (57.1 %)	9/12 (75.0 %)	19/24 (79.2 %)	0.333
female	6 /6(100.0 %)	2 /8(25.0 %)	2 /7(28.6 %)	**0.010***
Underlying diseases				
Hypertension	5/7 (71.4 %)	2/5 (40.0 %)	8/12 (66.7 %)	0.495
Diabetes	6 /8(75.0 %)	5/9 (55.6 %)	10/13 (76.9 %)	0.526
Hepatic disorders	5/7 (71.4 %)	4/10 (40.0 %)	11/18 (61.1 %)	0.387
Renal disorders	8/10 (80 %)	8/17 (47.1 %)	9/15 (60.0 %)	0.242
Malignant tumor	5/7 (71.4 %)	1/3 (33.3 %)	2/3 (66.7 %)	0.514
immunodeficiency disease	4/5 (80.0 %)	1/4 (25.0)	8/10 (80.0 %)	0.11
Previous dialysis	1/1 (100.0 %)	0 (0.0 %)	1/1 (100.0 %)	0.223
Diagnostic certainty				
Proven	4/8 (50.0 %)	8/14 (57.1 %)	6/13 (46.2 %)	0.846
Probable	3/3 (100.0 %)	0 (0.0 %)	3/4 (75.0 %)	1.000
Possible	7/9 (77.8 %)	3/6 (50.0 %)	14/14 (100.0 %)	**0.023***

* There was statistical difference between the cohorts.

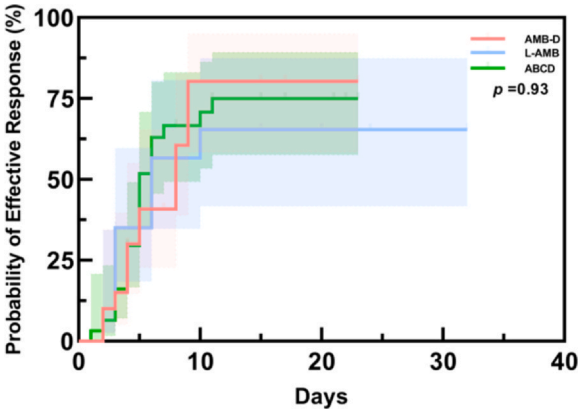

Fig. 2. KM analysis of effective rate among different amphotericin B.

Comparison of safety

Adverse events were observed in 69.0 % of participants (49 of 71). Renal injury emerged as the most frequent complication (43.7 %, 31/71), followed by hepatic injury (25.4 %, 18/71) , thrombocytopenia (23.9 %, 17/71) and hypokalemia (12.7 %, 9/71) ($p < 0.001$). No significant differences were observed in the overall incidence of adverse reactions across the three formulations. However, compared with other adverse reactions, the incidence of renal injury was significantly higher in the AMB-D group ($p = 0.05$), AMB-L group ($p = 0.018$), and ABCD cohort (p = 0.048) (Fig. 5). We further compared the timing of adverse drug reactions and found no significant differences (Fig. 4).

Comparison of economy

As depicted in Table 3. The AMB-D cohort incurred the most economical total cost ($p < 0.01$) and daily cost ($p < 0.01$) of amphotericin B. Furthermore, cost-effectiveness ratio analysis revealed a distinct advantage for the AMB-D regimen.

Discussion

This study enrolled 71 patients to evaluate the efficacy, safety, and economy of different amphotericin B formulations in the treatment of invasive fungal disease. The patient cohort demonstrated a high prevalence of underlying comorbidities, with renal disorders, diabetes mellitus and hypertension emerging as the most prevalent conditions, consistent with prior reports.[16,17] Notably, patients with pre-existing renal impairment were more frequently prescribed L-AMB therapy ($p = 0.021$), suggesting that renal characteristic may influence clinical decision-making on the chosen of amphotericin B formulations.[18] This therapeutic preference was supported by significantly higher serum creatinine levels observed in the L-AMB cohort ($p = 0.043$). Additionally, our analysis revealed Aspergillus and Mucorales as the predominant fungal pathogens, aligning with epidemiological patterns documented in European studies on invasive fungal infections.[19,20] Regarding the sites of fungal detection, although a higher number of fungal strains were detected in urine, fungi were also detected in the patient's sputum and blood. In this study, no patients were treated solely based on the detection of fungi in urine.

Published studies report complete response rates of 51 % for invasive fungal diseases (IFD) and 70.2 % for febrile neutropenia with

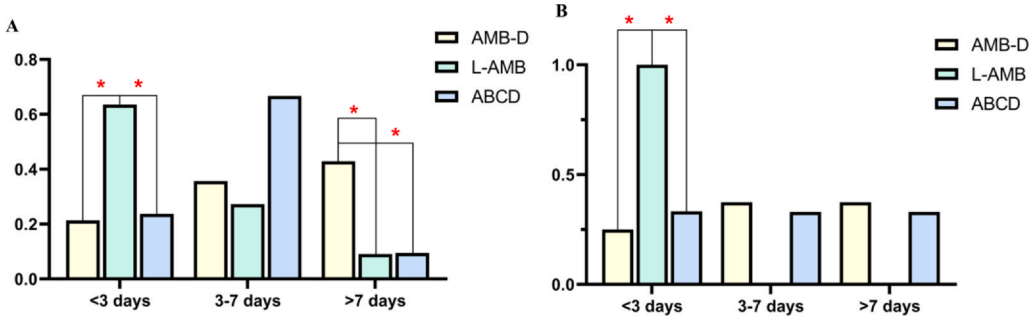

Fig. 3. Response rates of different amphotericin B in effective response cohort (A) and complete response cohort (B). * means $p < 0.05$.

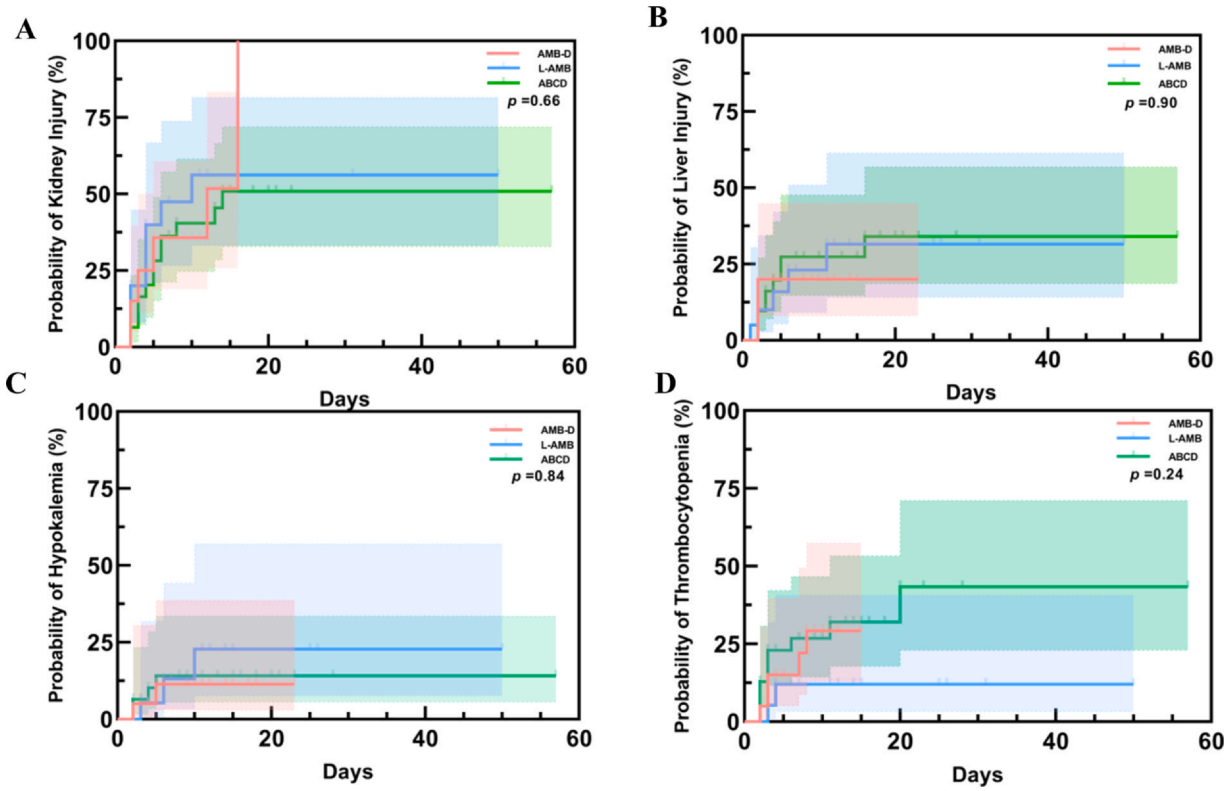

Fig. 4. KM analysis of drug adverse events among different amphotericin B.

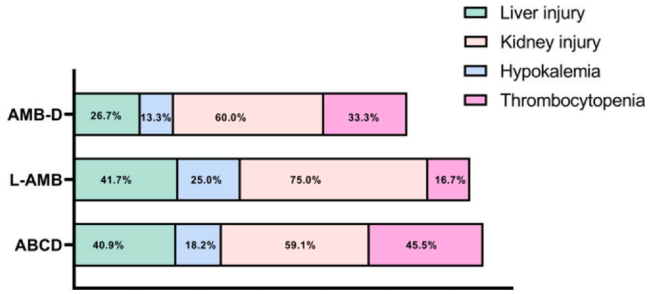

Fig. 5. Drug adverse events of different amphotericin B.

amphotericin B (AMB) therapy,[21,22] consistent with our observations. In this retrospective cohort study of 71 Chinese IFD patients, we concluded an effect response rate (complete/partial responses) of 64.8 %. However, no statistically significant differences in efficacy emerged among the three AMB formulations (70.0 % vs 55.0 % vs 67.7 %, $p = 0.55$). Comparative analyses by Keisuke Umemura et al.[23]demonstrated equivalent efficacy between L-AMB and AMB-D in preventing IFD following lung transplantation. While Cavassin et al.[21]initially reported superior overall success rates for ABLC compared to AMB-D and L-AMB, subsequent subgroup analysis of proven and probable cases revealed no significant inter-formulation differences. These findings align with a comprehensive meta-analysis of 25 randomized controlled trials (RCTs), which found no statistically significant variations in either therapeutic efficacy or mortality rates among the all four AMB formulations.[24] Collectively, these clinical data suggest similar therapeutic performance across different AMB preparations.

In contrast to previous investigations, our study innovatively demonstrates that L-AMB exhibits inferior efficacy in elderly populations, whereas AMB-D demonstrates enhanced effectiveness in female patients. Existing literature has indicated that L-AMB confers clinical advantages over AMB-D in HIV/AIDS patients.[25,26] Based on these findings, we recommend clinical decision-making regarding amphotericin B formulations should incorporate both demographic profiles and clinical presentations. Of particular significance, L-AMB achieved significantly higher response rates within 3 days compared to other formulations in both effective response ($p = 0.042$) and complete response cohorts ($p = 0.026$), suggesting accelerated therapeutic onset. Jadhav MP et al. also reported a similar conclusion.[22] Conversely, AMB-D demonstrated superior 7-day response rates in the effective response cohort ($p = 0.031$), indicative of delayed therapeutic effect. The clinical application of AMB-D remains constrained to low-dose regimens due to its nephrotoxicity. Pharmacokinetic studies demonstrate the high protein binding within its pharmacokinetic profile,[27] substantially compromising free drug concentration and potentially explaining the delayed therapeutic onset. ABCD is rapidly sequestered by the mononuclear phagocyte system due to its macromolecular structure, leading to lower plasma drug concentrations.[5] In contrast, L-AMB permits higher dosing regimens, reduced susceptibility to phagocytic

Table 3
Economic evaluation of different amphotericin B formulations.

	AMB-D	L-AMB	ABCD	*p*
Total cost	975.00 (468.75, 2006.25)	11505.00 (3237.50, 16962.50)	12276.00 (3564.00, 21780.00)	< 0.01
Daily cost	139.28 (80.20, 269.81)	1668.63 (956.09, 2638.48)	1334.35 (1018.29, 1849.09)	< 0.01
Cost/effectiveness	1392.86	20918.18	18132.94	

clearance, and selective affinity for fungal ergosterol over mammalian cholesterol,[5,28] hence the accelerated therapeutic onset. These findings collectively suggest L-AMB should be prioritized in critical care settings and emergency scenarios requiring rapid intervention.

Extensive research has established that amphotericin B is predominantly associated with hypokalemia, hepatotoxicity, nephrotoxicity, hematotoxicity, and infusion-related reactions.[10,23] Nevertheless, consensus regarding the comparative safety profiles of different formulations remains elusive. Previous studies have proposed reduced nephrotoxicity in L-AMB and ABCD compared to AMB-D[23,24] , with additional reports of shorter hospitalization duration and lower mortality rates in L-AMB recipients.[26] Tan et al.[25] observed significantly elevated hepatotoxicity and hematotoxicity rates in ABCD cohort relative to AMB-D and L-AMB, while Nokura et al. reported similar nephrotoxicity between L-AMB and AMB-D formulations.[10] Consistent with earlier clinical observations, our analysis demonstrates nephrotoxicity as the predominant adverse event (43.7 %), followed by hepatotoxicity (25.4 %),thrombocytopenia(23.9 %) and hypokalemia (12.7 %), with no statistically significant inter-group differences in adverse event incidence. However, interpretation of these findings requires caution due to potential selection bias, as patients with compromised baseline renal function at admission preferentially received L-AMB. Pharmacokinetic properties may explain formulation-specific toxicity profiles: liposomal encapsulation facilitates targeted drug delivery to infection sites via mononuclear phagocyte system uptake, thereby reducing renal exposure and subsequent nephrotoxic potential.[29] It is noteworthy that our data show the probability of nephrotoxicity was significantly higher in all three groups compared with other adverse reactions. However, L-AMB is still recommended as the first-choice drug for patients with renal insufficiency.

Pharmacoeconomic evaluations comparing different amphotericin B formulations remain limited in current literature. Umemura et al. demonstrated that L-AMB was associated with lower daily treatment costs compared to AMB-D for antifungal prophylaxis following lung transplantation.[23] Lobo Borba et al. developed a decision tree model suggesting AMB-D as the most cost-effective option for invasive fungal disease treatment, followed by L-AMB and ABLC.[30] Similar to the results of Lobo Borba et al., our analysis of real-world clinical data from 71 patients revealed AMB-D probably be the most economical choice to treat IFD.

We acknowledge several limitations in this study. The retrospective observational design and single-center nature of the research may conduct the generalizability pessimistic. Furthermore, the modest sample size prevented meaningful analysis of ABLC-related outcomes due to insufficient statistical power. Future investigations should prioritize prospective study designs utilizing larger, multi-center cohorts to enable more comprehensive data collection and rigorous multivariate analyses. Nonetheless, our findings offer a reference for the clinical application of amphotericin B and underline the importance of Therapeutic drug monitoring.

Conclusion

Amphotericin B formulations should be tailored to patient characteristics. L-AMB is preferred for urgent cases, while AMB-D is suitable for financially limited patients. Renal function requires close monitoring during Amphotericin B therapy.

Declarations

Not applicable.

Authors' contributions

Shizhao Yuan: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Yan Liu: Supervision, Resources, Project administration, Funding acquisition. Shuoxian Jia: Supervision, Resources, Project administration, Funding acquisition. Yan Zhao: Project administration, Methodology, Investigation. Ziyi Wang: Project administration, Methodology, Investigation. Jing yu: Supervision, Resources, Project administration, Funding acquisition. Chunhua Zhou: Supervision, Resources, Project administration, Funding acquisition. Shuai Liu: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of the First Hospital of Hebei Medical University (No.20220447).

Consent for publication

All authors have read and approved the final manuscript, and consent to its publication.

Data availability

Detailed information can be provided by the corresponding author upon reasonable request.

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Declaration of Competing Interest

The authors confirm that the funding had no infuence on the study results. There are no conficts of interest associated with this publication.

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Authors' other information

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References

1. Denning DW. Global incidence and mortality of severe fungal disease. *Lancet Infect Dis.* 2024;24:e428–e438.
2. Oa C, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the european confederation of medical mycology in cooperation with the mycoses study group education and research consortium. *Lancet Infect Dis.* 2019;19.
3. Pappas PG, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of america. *Clin Infect Dis.* 2016;62:e1–e50.
4. Cavassin FB, Baú-Carneiro JL, Vilas-Boas RR, Queiroz-Telles F. Sixty years of amphotericin B: an overview of the main antifungal agent used to treat invasive fungal infections. *Infect Dis Ther.* 2021;10:115–147.
5. Medical Mycology Society of Chinese Medicine and Education Association. Multidisciplinary expert consensus on the clinical rational application of different formulations of amphotericin B (2024 edition). Chinese Journal of Internal Medicine 63, 230–257 (2024).
6. Bekersky I, et al. Pharmacokinetics, excretion, and mass balance of liposomal amphotericin b (AmBisome) and amphotericin b deoxycholate in humans. *Antimicrob Agents Chemother.* 2002;46:828–833.
7. Groll AH, et al. Comparative efficacy and distribution of lipid formulations of amphotericin b in experimental candida albicans infection of the central nervous system. *J Infect Dis.* 2000;182:274–282.
8. Jadhav MP, et al. A randomized comparative trial evaluating the safety and efficacy of liposomal amphotericin b (Fungisome) versus conventional amphotericin b in the empirical treatment of febrile neutropenia in India. *Indian J Cancer.* 2012;49:107–113.

9. Falci DR, da Rosa FB, Pasqualotto AC. Comparison of nephrotoxicity associated to different lipid formulations of amphotericin B: a real-life study. *Mycoses.* 2015;58:104–112.
10. Nokura Y, et al. Comparison of adverse event profiles of amphotericin b formulations using Real-World data. *Cureus.* 2024;16:e71588.
11. Donnelly JP, et al. Revision and update of the consensus definitions of invasive fungal disease from the european organization for research and treatment of cancer and the mycoses study group education and research consortium. *Clin Infect Dis.* 2020;71:1367–1376.
12. Qin J, et al. Real-World effectiveness and safety of isavuconazole versus amphotericin b for patients with invasive mucormycosis. *Microorganisms.* 2025;13:55.
13. Boogaerts M, et al. Intravenous and oral itraconazole versus intravenous amphotericin b deoxycholate as empirical antifungal therapy for persistent fever in neutropenic patients with cancer who are receiving Broad-Spectrum antibacterial therapy: a randomized, controlled trial. *Ann Intern Med.* 2001;135:412–422.
14. Lopez-Berestein G, et al. Treatment of systemic fungal infections with liposomal amphotericin b. *Arch Intern Med.* 1989;149:2533–2536.
15. Yigeng Cao, et al. Safety and efficacy of amphotericin b colloidal dispersion in the salvage treatment of invasive fungal disease. *Chin J Infect Chemother.* 2023;23:443–448.
16. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. *JoF.* 2019;5:26.
17. Özbek L, et al. COVID-19–associated mucormycosis: a systematic review and meta-analysis of 958 cases. *Clin Microbiol Infect.* 2023;29:722–731.
18. Mesa-Arango AC, Scorzoni L. & zaragoza, O. It only takes one to do many jobs: amphotericin b as antifungal and immunomodulatory drug. *Front Micro.* 2012;3.
19. von Lilienfeld-Toal M, Wagener J, Einsele H, Cornely OA, Kurzai O. Invasive fungal infection. *Dtsch Arztebl Int.* 2019;116:271–278.
20. Lass-Flörl C, Steixner S. The changing epidemiology of fungal infections. *Mol Asp Med.* 2023;94:101215.
21. Cavassin FB, et al. Effectiveness, tolerability, and safety of different amphotericin b formulations in invasive fungal infections: a multicenter, retrospective, observational study. *Clin Ther.* 2024;46:322–337.
22. Jadhav M, et al. A randomized comparative trial evaluating the safety and efficacy of liposomal amphotericin b (Fungisome™) versus conventional amphotericin b in the empirical treatment of febrile neutropenia in India. *Indian J Cancer.* 2012;49:107.
23. Umemura K, et al. Comparison of the safety and cost-effectiveness of nebulized liposomal amphotericin b and amphotericin b deoxycholate for antifungal prophylaxis after lung transplantation. *J Infect Chemother.* 2024;30:741–745.
24. Tonin FS, et al. Efficacy and safety of amphotericin b formulations: a network meta-analysis and a multicriteria decision analysis. *J Pharm Pharmacol.* 2017;69:1672–1683.
25. Tan Y, et al. Safety of different amphotericin b formulations among AIDS patients with invasive fungal disease: a retrospective observational study. *AIDS Res Ther.* 2024;21:66.
26. Falci DR, Da Rosa FB, Pasqualotto AC. Comparison of nephrotoxicity associated to different lipid formulations of amphotericin B: a real-life study. *Mycoses.* 2015;58:104–112.
27. Bekersky I, et al. Plasma protein binding of amphotericin b and pharmacokinetics of bound versus unbound amphotericin b after administration of intravenous liposomal amphotericin b (AmBisome) and amphotericin b deoxycholate. *Antimicrob Agents Chemother.* 2002;46:834–840.
28. Faustino C, Pinheiro L. Lipid systems for the delivery of amphotericin b in antifungal therapy. *Pharmaceutics.* 2020;12:29.
29. Botero Aguirre JP, Restrepo Hamid AM. Amphotericin b deoxycholate versus liposomal amphotericin B: effects on kidney function. *Cochrane Database Syst Rev.* 2015;2015:CD010481.
30. Lobo Borba HH, et al. Cost-effectiveness of amphotericin b formulations in the treatment of systemic fungal infections. *Mycoses.* 2018;61:754–763.