INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Paper

Cost-Effectiveness Analysis of L-Asparaginase versus PEG-Asparaginase in the Treatment Regimen of Acute Lymphoblastic Leukemia

Omkar Shedbale[1], Manjula G.*[2], Ashwini Doddannavar[3]

[1]Dept.of Pharmacy Practice KLE College of Pharmacy-Belagavi, KLE Academy for Higher Education and Research (KAHER) Belagavi, Karnataka, India-590010.

*[*2,3] Assistant Professor, Dept.of Pharmacy Practice KLE College of Pharmacy-Belagavi, KLE Academy for Higher Education and Research (KAHER) Belagavi, Karnataka, India-590010*

ARTICLE INFO

Published: 08 June 2025

Keywords:
Acute lymphoblastic leukemia, PEG-asparaginase, L-asparaginase, cost-effectiveness analysis, Pharmacoeconomics, pediatric oncology, ICER.

DOI:
10.5281/zenodo.15619127

ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer, with asparaginase-based regimens forming the backbone of therapy. While both PEG-asparaginase and L-asparaginase are commonly employed, they differ significantly in pricing, drug metabolism, and dosing frequency. This study evaluates the economic efficiency of PEG-asparaginase relative to L-asparaginase for pediatric ALL treatment. Method: This pharmacoeconomic evaluation included 55 pediatric ALL patients, with treatment distribution as follows: 50 received PEG-asparaginase, 9 received L-asparaginase, and 4 patients were treated with both agents. Therapeutic efficacy was assessed using an established clinical outcome metric, while direct medical expenditures were systematically documented. The economic evaluation incorporated calculation of the incremental cost-effectiveness ratio (ICER). Statistical comparisons of cost and effectiveness measures were performed using independent sample t-tests, and variable relationships were examined through Pearson correlation analysis. Result: The average cost per patient for PEG-asparaginase was INR. 27,960.00, compared to INR. 2,244.40 for L-asparaginase. Mean effectiveness scores were 0.97 and 0.68, respectively. The ICER for PEG-asparaginase versus L-asparaginase was calculated at INR. 88,674.48 per unit of effectiveness gained. The difference in cost between the two treatments was statistically significant ($p = 0.008$), while the difference in effectiveness was not ($p = 0.436$). Pearson correlation analysis indicated a significant positive correlation between drug type and cost ($r = 0.525$, $p < 0.001$), but not between cost and

***Corresponding Author:** Manjula G.
Address: *Dept.of Pharmacy Practice KLE College of Pharmacy-Belagavi, KLE Academy for Higher Education and Research (KAHER) Belagavi, Karnataka, India-590010*
Email ✉: manjulag@klepharm.edu

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

effectiveness (r = 0.084, p = 0.529). Conclusion: While PEG-asparaginase demonstrated slightly higher clinical effectiveness, its significantly higher cost did not yield a statistically significant improvement in outcomes over L-asparaginase. These findings suggest that L-asparaginase may offer a more cost-effective option for pediatric ALL treatment, particularly in resource-limited settings. Further research with larger sample sizes is recommended to validate these results.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy, accounting for approximately 25% of all childhood cancers globally. [1] Over the past decades, significant advancements in multi-agent chemotherapy protocols have led to remarkable improvements in survival outcomes, with cure rates exceeding 85% in developed countries. [2] A cornerstone of contemporary ALL treatment is the inclusion of asparaginase, an enzyme-based therapy that depletes extracellular asparagine, an amino acid critical for leukemic cell survival. [3]

Two primary asparaginase formulations are utilized clinically: native Escherichia coli L-asparaginase (L-Asp) and its pegylated version (PEG-Asp). The pegylated form is engineered by conjugating polyethylene glycol to the native enzyme, enhancing its stability in the bloodstream and lowering immune reactivity. This modification permits extended dosing intervals and may lead to better treatment compliance. [4] Despite its benefits, PEG-asparaginase carries a substantially higher price tag compared to the conventional L-asparaginase, prompting questions about its economic feasibility - especially in healthcare systems with limited resources.

Pharmacoeconomic assessments, including cost-effectiveness analyses (CEA), serve as critical instruments for informing health policy, enhancing resource distribution, and facilitating data-driven clinical decisions. These evaluations hold particular significance in pediatric oncology, where expensive cancer therapies and their lasting impact on both patient prognosis and healthcare infrastructure necessitate careful economic consideration. [5]

The increasing burden of healthcare costs globally has made it essential to adopt a more systematic method for analyzing the economic effects of medical treatments. Pharmacoeconomics, a specialized branch of health economics, is vital in determining the value of drugs and therapies by weighing their expenses against their outcomes. Within pharmacoeconomic assessment, cost-effectiveness analysis (CEA) stands out as a key technique, helping policymakers allocate constrained healthcare resources efficiently to achieve optimal health outcomes. [6]

Cost-effectiveness analysis (CEA) evaluates different medical interventions by assessing their expenses relative to their health benefits, often measured as cost per quality-adjusted life year (QALY) or cost per life year gained (LYG). This approach is especially valuable when comparing treatments with similar effectiveness but varying costs, or those with differing outcomes but comparable expenses. By providing a structured way to assess value, CEA helps policymakers, insurers, and healthcare systems prioritize cost-efficient treatments, ensuring that limited resources are allocated to interventions that deliver the greatest health benefits per dollar spent. [6]

While pediatric ALL treatment achieves cure rates exceeding 80% in developed nations, significant treatment outcome gaps persist across resource-limited settings. In many Low-and middle-income countries (LMICs), childhood ALL survival outcomes remain suboptimal, with five-year survival estimates ranging between just 30% to 50% in some regions. [7] Several key challenges contribute to these disparities, including medication shortages, treatment discontinuations caused by economic barriers, inadequate supportive care systems, and variable treatment

guidelines. In resource-limited settings, the economic impact of cancer care presents particular difficulties, as patients frequently face substantial personal expenses for therapy, while public healthcare systems may not provide complete coverage for costly treatments like PEG-asparaginase. [8] A critical consideration—especially in resource-limited settings—is whether PEG-asparaginase therapeutic advantages warrant its substantially greater expense relative to conventional L-asparaginase. Cost-effectiveness analyses (CEAs) serve as vital instruments in healthcare economics, evaluating not only clinical efficacy but also the economic justification of therapeutic interventions. These assessments prove indispensable for LMIC healthcare administrators and policy makers when determining optimal treatment protocols that must weigh clinical benefits against potential adverse effects while maintaining fiscal responsibility within constrained healthcare budgets. [5]

METHOD AND MATERIALS

2.1. Study design and Site

Prospective, observational research was conducted between September 2024 to February 2025 at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi. During this study reviewed the patient files or patient's health records of pediatric subjects diagnosed with ALL and also patients received one dose of L-Asparaginase or PEG-Asparaginase dose during this timeframe. The research protocol was reviewed and approved by the Institutional Review Board for clinical research (Ref No. KLECOPBGMEC/D015-2024, dated 30 August 2024).

2.2. Selection Criteria

Both Male and Female patients diagnosed with Acute lymphoblastic leukemia (ALL) undergone L-Asparaginase, PEG-Asparaginase or both in L-asparaginase and PEG-asparaginase treatment of age group 0 to 18 years were included in the study. Whereas subjects who are not willing to give informed consent and assent are excluded from the study.

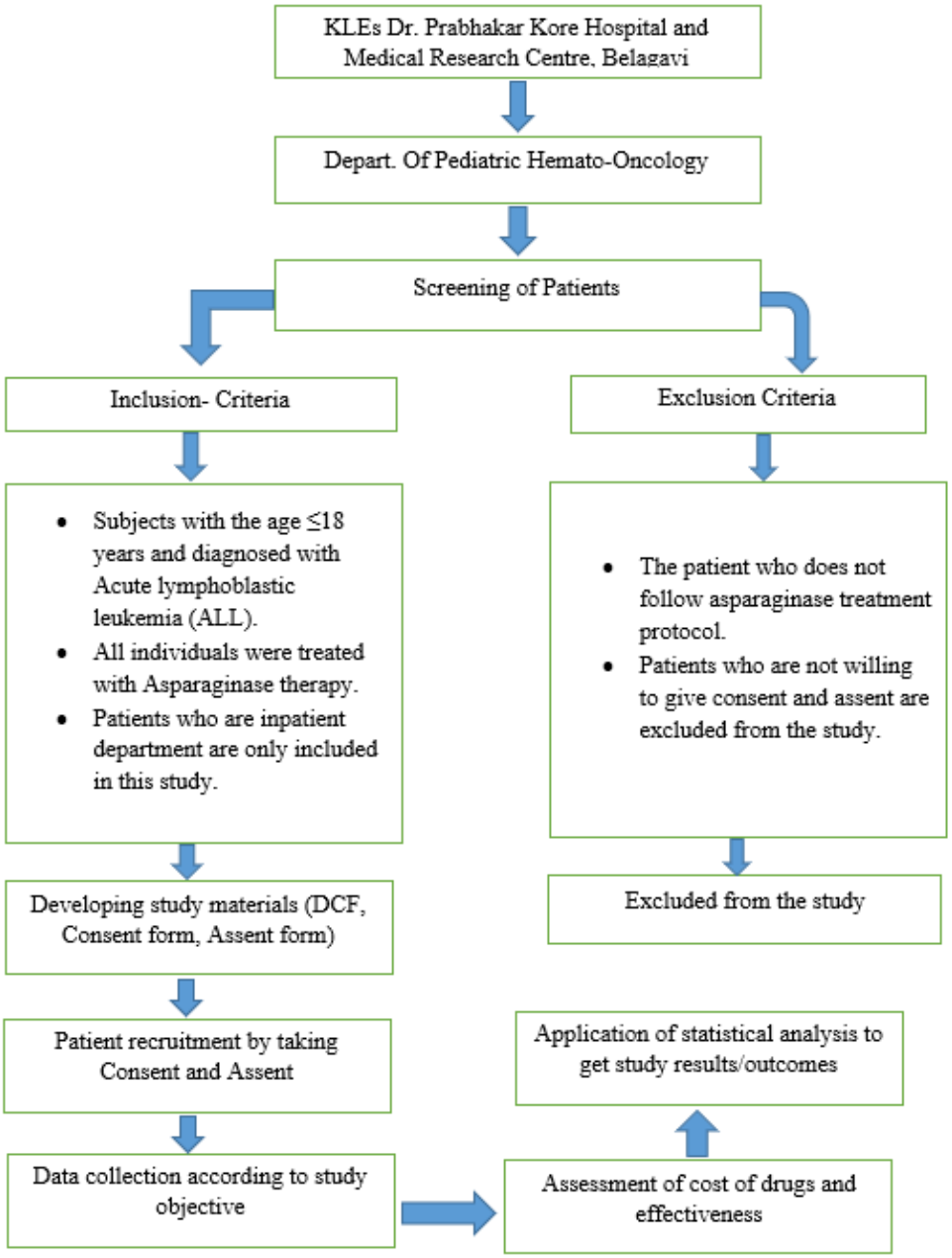
2.3. Data Collection

Demographics data is collected that includes Patient's Age, Gender, Body weight, Height, Type of ALL, Phase of ALL, Risk stratification, L-ASP or PEG-ASP dose, Cost of Drug.

2.4. Statistical analysis

Statistical analysis was done by using SPSS version 20 software. Descriptive analysis was performed by calculating percentages and frequencies of variables. Independent sample t-test is used Comparison of Cost and Effectiveness Between PEG-Asparaginase and L-Asparaginase and Parson Correlation test is used to determine the correlation among Cost, Effectiveness and Type of Asparaginase administered.

Figure 1. Research Process flowchart



RESULTS

Table no.1: Patients demographics and clinical characteristics (n=55)

Characteristics	Variables	Frequency (n)	Percentage (%)
Age	0-5	17	30.9
	6-10	**19**	**34.5**
	11-15	15	27.3

	16-18	4	7.3
Gender	Male	**37**	**67.3**
	Female	18	32.7
Diagnosis	Pre β-ALL	**36**	**65.5**
	T-Cell ALL	13	23.6
	Relapse Pre β-ALL	4	7.3
	Mixed phenotype ALL	2	3.6
Treatment Phase	Induction phase	**37**	**67.3**
	Consolidation phase	15	27.3
	Delayed Intensification phase	2	3.6
	Maintenance Phase	1	1.8
Risk Stratification	Intermediate risk	**34**	**61.8**
	High Risk	21	38.2
Type of Asparaginase treatment	L-Asparaginase	5	9.09
	PEG-Asparaginase	**46**	**83.6**
	L-ASP+PEG-ASP	4	7.3
Asparaginase Cut-off Dose	≤2500	22	40
	>2500	**33**	**60**
Toxicity Incidence	Patients with toxicities	**48**	**87.27**
	Patients without toxicities	07	12.73
Income Scale (BGP scale)	Class-I	**36**	**65.45**
	Class-II	11	20.00
	Class-III	4	7.27
	Class-IV	4	7.27
	Class-V	0	0

Fifty-five Individuals with ALL were included in the study, majority of cases were male 67.3% (n=37), the majority of patients found in age group 6-10 yrs., 34.5% (n=19). In terms of disease 65.5% (n=36) patients were diagnosed with pre β-ALL, 23.6% (n=13) were T-cell ALL, 7.3% (n=4) were Relapse pre β-ALL and 3.6% (n=2) were Mixed phenotype ALL. Among 55 patients 67.3% (n=37) were undergone Induction phase, 27.3% (n=15) of consolidation phase, 3.6% (n=2) of Delayed intensification phase and 1.8% (n=1) of maintenance phase. According to risk 61.8% (n=34) were intermediate risk and 38.2% (n=21) were high risk. 3 types of asparaginase chemotherapy was administered to the patient out of that 83.6% (n=46) of PEG-Asparaginase was administered, 9.09% (n=5) of L-Asparaginase and 7.3% (n=4) of both L-Asparaginase and PEG asparaginase chemotherapy was given to patients. Furthermore 60%(n=33) patients were administered >2500 IU of asparaginase dose and 40% (n=22) patients were administered <2500 IU. (refer Table no.1).

Table no.2: Cost, Effectiveness and Incremental Cost-Effectiveness Ratio (ICER) of PEG-Asparaginase vs L-Asparaginase. (n=59)

Type of Drug	No. of patients	Avg. Cost	Avg. Effectiveness	ICER CostA-CostB/Effect A-Effect B
PEG-Asp	50	27960.00	0.97	**88674.48**
L-Asp	9	2244.40	0.68	
Difference		**25715.60**	**0.29**	

The study included a total 55 patients. Out of these, 50 received PEG-asparaginase and 9 were treated with L-asparaginase. Notably, 4 patients received both PEG-asparaginase and L-asparaginase during the treatment course and were therefore included in the analysis for both groups based on respective drug received.

The mean treatment cost per patient was INR 27,960.00 for PEG-asparaginase and INR 2,244.40 for L-Asparaginase. In terms of therapeutic effectiveness, PEG-asparaginase demonstrated a higher average score of 0.97, compared to 0.68 for L-asparaginase. This resulted in an incremental effectiveness of 0.29 between the two treatments.

The difference in cost between the two drugs was INR 25,715.60. Using these values, the Incremental Cost-Effectiveness Ratio (ICER) was determines as,

$$ICER = \frac{27,960.00 - 2,244.40}{0.97 - 0.68}$$

$$= INR.\ 88674.48$$

The ICER indicates that the use of PEG-asparaginase incurs an additional cost of INR 88674.48 for each unit increase in effectiveness when compared to L-asparaginase.

Table no.3: Comparison of Cost and Effectiveness Between PEG-Asparaginase and L-Asparaginase Using Independent Sample t-Test.

	Type of Drug	No. of Patients (N)	Mean	Standard deviation	t-test	p-Value
Effectiveness	Peg-Asparaginase	50	0.783	0.142	0.485	0.436
	L-asparaginase	9	0.760	0.071	0.759	
Cost	Peg-Asparaginase	50	27800	16348.25	4.65	0.008*
	L-asparaginase	9	2244.40	798.6	10.98	

*Independent Sample t-test

An independent samples t-test was applied to assess differences in both effectiveness and cost between patients treated with PEG-asparaginase and those who received L-asparaginase.

The analysis showed that the **mean effectiveness** for the PEG-asparaginase group (n = 50) was 0.783 (SD = 0.142), compared to 0.760 (SD = 0.071) for the L-asparaginase group (n = 9). This difference in effectiveness was not statistically significant, t (57) = 0.485, p = 0.436.

In contrast, the **cost analysis** revealed a significant difference between the two groups. The average cost of treatment for patients administered PEG-asparaginase was USD 27,800.00 (SD = 16,348.25), whereas the cost for those treated with L-asparaginase was considerably lower, at USD

2,244.40 (SD = 798.60). The difference in cost was statistically significant, t (57) = 4.65, p = 0.008. These results suggest that while the effectiveness between the two treatment groups was comparable, PEG-asparaginase was associated with a significantly higher financial burden.

Table no.4: Pearson Correlation among Cost, Effectiveness and Type of Asparaginase administered.

	Cost	Effectiveness	Type of Drug
Cost Pearson Correlation p-Value	1	0.84 0.529	0.525 0.000
Effectiveness Pearson Correlation p-Value	0.08 0.529	1	0.64 0.629
Type of Drug Pearson Correlation p-Value	0.525 0.00	0.64 0.629	1

*Person Correlation

To evaluate the relationships between treatment cost, effectiveness, and the type of asparaginase used, a Pearson correlation analysis was conducted.

A **moderate to strong positive correlation** was identified between the **drug type** and **cost** (r = 0.525), which was found to be statistically significant ($p < 0.001$). This indicates that the cost of treatment varied significantly depending on whether PEG-asparaginase or L-asparaginase was used, with PEG-asparaginase being associated with higher treatment expenses.

There was also a **positive correlation** between **drug type** and **treatment effectiveness** (r = 0.640); however, this association was not statistically significant ($p = 0.629$), suggesting no conclusive evidence that drug type directly influenced treatment outcomes in this cohort.

Additionally, the correlation between **cost** and **effectiveness** was weak (r = 0.084) and not statistically significant ($p = 0.529$), indicating that increased spending did not necessarily correspond with improved clinical outcomes.

DISCUSSION

This pharmacoeconomic analysis evaluated the cost-effectiveness of PEG-asparaginase compared to native L-asparaginase for treating pediatric acute lymphoblastic leukemia (ALL). Although PEG-asparaginase demonstrated a marginally higher mean effectiveness (0.97 vs. 0.68), the difference was not statistically significant (p = 0.436). In contrast, the cost disparity was considerable and statistically significant (p = 0.008), with PEG-asparaginase costing INR 27,960.00 per patient on average, while L-asparaginase was significantly cheaper at INR 2,244.40. The incremental cost-effectiveness ratio (ICER) of INR 88,674.48 per effectiveness unit highlights the substantial additional expense of PEG-asparaginase without a commensurate clinical benefit. These findings align with previous study, who found that while PEG-asparaginase was associated with improved pharmacokinetics and longer asparagine depletion, this did not always translate into significantly better clinical outcomes, especially in standard-risk patients. [9]

This study ICER results aligns with a previous study conducted by Kumar et al. who reported an ICER of INR 81,000 for PEG-asparaginase versus L-asparaginase in a pediatric ALL patients and concluded that native L-asparaginase was more cost-effective for low-risk groups. [10] Additionally, Neumann et al. highlighted that therapies with minor effectiveness often lead to

disproportionately high ICERs, making them economically viable only when accompanied by meaningful survival of QOL benefits. [5] This current study finding add to the existing evidence that PEG-asparaginase may be best reserved for specific cases particularly high-risk or relapsed patients, as well as those with hypersensitivity to the native form. While 87.27% of patients in our study developed toxicities (without differentiation between formulations), future studies should investigate whether PEG-asparaginase lowers adverse event rates, which could otherwise lead to increased treatment expenses.

PEG-asparaginase, a pegylated version of the enzyme, was developed to minimize immunogenic reactions and prolong its half-life, enabling less frequent administration and better treatment compliance. Previous study by Panosyan et al. (2004) and Avramis et al. (2005) demonstrated that this modified formulation sustains effective asparagine depletion for extended periods, which may enhance therapeutic outcomes while lowering hypersensitivity risks. [11,3] Nevertheless, real-world clinical benefits in terms of long-term survival do not always show significant advantages over conventional L-asparaginase, especially in low-risk or standard-risk pediatric ALL cases.

Toxicity represents a critical consideration in asparaginase-based treatment regimens. While our investigation observed substantial treatment-related adverse events (87.27% overall incidence), we did not differentiate these occurrences between the two formulations. Earlier research by Tong et al. (2013) suggested that PEG-asparaginase may offer advantages in terms of reduced allergic reactions and possibly fewer hypersensitivity-related hospitalizations, potentially yielding economic benefits through decreased supportive care requirements. However, our current study did not specifically evaluate these potential cost-saving aspects. [12]

CONCLUSION

This pharmacoeconomic analysis compared PEG-asparaginase and L-asparaginase for pediatric ALL treatment. The results showed marginally better clinical outcomes with PEG-asparaginase, though this advantage lacked statistical significance. More strikingly, PEG-asparaginase's treatment costs exceeded those of L-asparaginase by a factor of ten, a difference that was statistically robust. The calculated ICER of INR 88,674.48 per effectiveness unit gain underscores the significant financial implications of choosing the pegylated formulation. The evidence indicates L-asparaginase presents a more economically viable choice, particularly valuable in resource-constrained healthcare systems where cost considerations critically influence treatment availability and patient compliance. While PEG-asparaginase maintains clinical relevance for specific cases such as patients needing reduced dosing frequency or those with native formulation intolerance its widespread adoption appears economically unsustainable in low- and middle-income country settings without substantial clinical justification. The findings advocate for judicious, patient-specific utilization of the more expensive formulation rather than routine application.

Conflict of Interest

The author (s) declare that they have no potential conflict of interest

Funding

No funding's were received for this study. The research was conducted independently without financial support from any funding agency, commercial entity or non-profit organization.

Acknowledgments

We sincerely thank to Pediatric Hemato-oncology Department for their invaluable support and guidance throughout this study also thankful to all the study participants for their voluntarily participation in this study. We extend our gratitude to KLES College of Pharmacy, Belagavi, KAHER-Belagavi and KLE's Dr. Prabhakar kore Hospital and MRC, Belagavi for providing the necessary facilities and resources to conduct this research. Their contributions and encouragement have been instrumental in this successful completion of this work.

Ethical clearance

The study was approved by Institutional Ethics committee of KLE college of pharmacy, Belagavi (Ref no. KLECOPBGMEC/D015-2024). The patient's identities were kept confidential and rewards were not provided to the participant.

REFERENCES

1. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. The Lancet. 2008 Mar 22;371(9617):1030-43.
2. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. New England Journal of Medicine. 2015 Oct 15;373(16):1541-52.
3. Avramis VI, Panosyan EH. Pharmacokinetic/pharmacodynamic relationships of asparaginase formulations: the past, the present and recommendations for the future. Clinical pharmacokinetics. 2005 Apr;44:367-93.
4. Burke AA. Targeting T-cells to Acute Myeloid Leukemia with a Novel Bispecific Antibody Format. Columbia University; 2022. Burke AA. Targeting T-cells to Acute Myeloid Leukemia with a Novel Bispecific Antibody Format. Columbia University; 2022.
5. Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats TG, editors. Cost-effectiveness in health and medicine. Oxford University Press; 2016 Oct 3.
6. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford university press; 2015 Sep 25.
7. Mostert S, Sitaresmi MN, Gundy CM, Sutaryo N, Veerman AJ. Influence of socioeconomic status on childhood acute lymphoblastic leukemia treatment in Indonesia. Pediatrics. 2006 Dec 1;118(6):e1600-6.
8. Israels T, Ribeiro RC, Molyneux EM. Strategies to improve care for children with cancer in Sub-Saharan Africa. European journal of cancer. 2010 Jul 1;46(11):1960-6.
9. Place AE, Stevenson KE, Vrooman LM, Harris MH, Hunt SK, O'Brien JE, Supko JG, Asselin BL, Athale UH, Clavell LA, Cole PD. Intravenous pegylated asparaginase versus intramuscular native Escherichia coli L-asparaginase in newly diagnosed childhood acute lymphoblastic leukaemia (DFCI 05-001): a randomised, open-label phase 3 trial. The lancet oncology. 2015 Dec 1;16(16):1677-90.
10. Kumar A, Nair A, Joseph T, et al. Economic evaluation of PEG-asparaginase in pediatric ALL: An Indian experience. Indian J Hematol Blood Transfus. 2022;38(1):88-95.
11. Panosyan EH, Grigoryan RS, Avramis IA, Avramis VI. Depletion of asparagine correlates with serum activity of PEG-asparaginase in therapy for ALL. Anticancer Res. 2004;24(4):2143-7.
12. Tong WH, Pieters R, Kaspers G, te Loo MD, Bierings M, van den Bos C, Kollen WJ, Hop WC, Boos J, Relling MV, Kuehnel HJ. A prospective study on drug monitoring of pegasparaginase and Erwinia asparaginase and

asparaginase antibodies in pediatric acute lymphoblastic leukemia. Blood. 2013 Nov 15;122(21):2634.

HOW TO CITE: Omkar Shedbale, Manjula G.*, Ashwini Doddannavar, Cost-Effectiveness Analysis of L-Asparaginase versus PEG-Asparaginase in the Treatment Regimen of Acute Lymphoblastic Leukemia, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 6, 1657-1666. https://doi.org/10.5281/zenodo.15619127