Original Research Paper

Volume - 15 | Issue - 08 | August - 2025 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Oncology

ORAL LOW-DOSE CHEMOTHERAPY IN PEDIATRIC ONCOLOGY: A REAL-WORLD STUDY ON FEASIBILITY AND OUTPATIENT ADHERENCE

Agnidipa Sanyamath	3rd Year Junior Resident, Department of Pharmacology, Medical College, Kolkata.
Debangee Mandal	1st Year Junior Resident, Department of Pharmacology, Medical College, Kolkata.
Swarnabindu Banerjee	HOD and Associate Professor, Department of Medical Oncology, Medical College, Kolkata.
Manab Nandy	Professor, Department of Pharmacology, Medical College, Kolkata.

ABSTRACT **Background:** In low- and middle-income countries (LMICs), pediatric oncology care is often limited by the high cost, toxicity, and infrastructure demands of conventional chemotherapy. Oral low-dose chemotherapy (OLDC) offers a potential solution by enabling continuous, home-based treatment with reduced resource dependence. This study evaluates the real-world feasibility, adherence, and outpatient tolerability of OLDC in children with relapsed or refractory malignancies. **Methods:** This prospective observational study included 133 pediatric patients aged 1–18 years with advanced solid or hematologic cancers, treated at the Departments of Medical Oncology and Pharmacology, Medical College Kolkata. All participants received a standardized oral low-dose chemotherapy protocol comprising rotating cycles of cyclophosphamide, methotrexate, etoposide, and 6-mercaptopurine. Patients were followed monthly for six months to assess treatment completion, adherence, interruptions, and outpatient feasibility. **Results:** The OLDC regimen was well tolerated and highly feasible in an outpatient setting. Over 92.5% of patients received treatment entirely on an outpatient basis, and 89.4% completed at least three full chemotherapy cycles. Adherence was strong, with only 9.8% of patients experiencing temporary dose interruptions, primarily due to mild, reversible toxicities. No patient required hospitalization solely for drug-related adverse events. Family-reported compliance and physician-recorded follow-up rates were consistently high, suggesting the acceptability and practicality of home-based oral therapy in a resource-constrained environment. **Conclusion:** This study demonstrates that oral low-dose chemotherapy is both feasible and well tolerated in pediatric patients with advanced cancers, with high adherence and minimal disruption in outpatient settings. These findings support broader adoption of OLDC as a viable therapeutic strategy in LMICs where access to intensive inpatient treatment is limited.

KEYWORDS : Pediatric oncology, oral chemotherapy, low-dose therapy, outpatient cancer care, adherence, feasibility, resource-limited settings

INTRODUCTION

Despite significant therapeutic advances, childhood cancer survival remains highly unequal across the globe. In low- and middle-income countries (LMICs), survival rates are disproportionately lower due to barriers such as late diagnosis, treatment abandonment, and lack of supportive infrastructure [1,2]. High-intensity intravenous chemotherapy, the mainstay of pediatric oncology, requires hospital-based administration, intensive monitoring, and significant financial resources- factors that often overwhelm under-resourced health systems [3,4].

To bridge this gap, alternative models of care have emerged that emphasize decentralization, reduced toxicity, and affordability. Among them, oral low-dose chemotherapy (OLDC) has shown promise as a feasible outpatient-based approach, particularly for children with relapsed, refractory, or palliative-stage malignancies [5–7]. OLDC involves continuous or cyclical administration of low-dose cytotoxic agents such as cyclophosphamide, methotrexate, etoposide, and 6-mercaptopurine, typically without hospitalization or IV access [8,9].

Unlike conventional chemotherapy, OLDC can be administered at home under supervision, which not only improves accessibility but also reduces direct and indirect treatment costs [10–12]. Studies from LMICs have shown that such regimens can be tolerated well, offer modest disease control, and are particularly suited for patients in whom curative therapy is no longer an option [13,14].

Yet, the real-world implementation of OLDC in pediatric oncology remains under-investigated. Existing literature is largely focused on toxicity and response rates, with limited attention given to practical outcomes like adherence, treatment completion, and outpatient feasibility, metrics essential for long-term integration into national cancer care programs [15–17]. In the absence of supportive infrastructure or caregiver training, even well-tolerated regimens may suffer from poor compliance, jeopardizing their utility [18].

In this context, our study evaluates the feasibility, adherence, and delivery outcomes of a structured OLDC regimen in a public tertiary care center in India. By focusing on regimen completion, dose interruptions, and outpatient continuity, we aim to assess the operational success of OLDC and its potential role in sustainable pediatric oncology care delivery in resource-limited environments.

AIMS AND OBJECTIVES

1. To evaluate the feasibility of administering oral low-dose chemotherapy (OLDC) in an outpatient setting to children with relapsed, refractory, or advanced-stage malignancies.
2.To assess treatment adherence, regimen completion, and frequency of dose interruptions in pediatric patients receiving OLDC over a six-month follow-up period.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective, observational study conducted at the Departments of Medical Oncology and Pharmacology, Medical College Kolkata, over a six-month period. The primary focus was to assess real-world feasibility and adherence to oral low-dose chemotherapy (OLDC) among pediatric oncology patients receiving care in a government tertiary center in eastern India.

Study Population And Ethics

Children aged 1 to 18 years with histologically or cytologically confirmed solid or hematologic malignancies, who were not candidates for curative-intent therapy, were enrolled. Patients with relapsed, refractory, or metastatic disease stages were eligible. Informed consent was obtained from parents or guardians, and assent was obtained from children aged above 7 years. The study was approved by the Institutional Ethics Committee and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

Inclusion And Exclusion Criteria

Inclusion criteria included pediatric patients (1–18 years) with relapsed or refractory malignancies, Eastern Cooperative Oncology Group (ECOG) performance status ≤2, adequate hepatic, renal, and bone marrow function, and an expected survival of at least 3 months. Patients were required to be capable of oral drug intake and have caregiver support for outpatient follow-up.

Exclusion criteria included major organ dysfunction (hepatic, renal, or

cardiac), active uncontrolled infections, inability to comply with monthly visits, known hypersensitivity to any study drug, pregnancy or lactation, and enrollment in another interventional trial.

Chemotherapy Regimen And Administration

All participants received a rotating OLDC protocol comprising:

- Cyclophosphamide: 25 mg/m²/day for 21 days
- Methotrexate: 10 mg/m² twice weekly
- Etoposide: 50 mg/m²/day for 21 days
- 6-Mercaptopurine: 50 mg/m²/day continuously

These drugs were administered as oral tablets or syrups, in 4-week rotating cycles, under supervision of caregivers at home. Dosing was reviewed monthly and adjusted based on tolerability and hematologic parameters. Treatment was planned entirely on an outpatient basis, with supportive medications provided as needed.

Adherence And Feasibility Assessment

The primary outcomes assessed included:

- Treatment completion rates (number of patients completing ≥3 cycles)
- Frequency of dose interruptions (defined as >3 consecutive missed doses due to toxicity or non-compliance)
- Outpatient delivery success (proportion receiving all cycles without inpatient admission)
- Follow-up retention (proportion of patients completing 6 months of monitoring)

Caregivers were educated on medication schedules and instructed to maintain daily dosing logs. Pill counts and verbal confirmation were used to verify adherence at each visit. Missed doses and temporary drug holds were documented by the treating team.

Statistical Analysis

Descriptive statistics were used to report adherence rates, treatment completion, and follow-up patterns. Categorical variables (e.g., cycle completion, interruptions) were summarized as frequencies and percentages. Associations between baseline factors and adherence outcomes were explored using Chi-square or Fisher's exact test, where appropriate. All statistical analyses were performed using IBM SPSS Statistics version 26, with $p < 0.05$ considered statistically significant.

RESULTS

Patient Demographics and Clinical Profile

A total of 133 pediatric patients were included in the study, with a mean age of 6.87 ± 3.17 years (range 1–18 years), and a male-to-female ratio of approximately 3:1 (99 males, 74.4%; 34 females, 25.6%). In our study, 42 % patients were 1-5 years of age, 48% patients were 6-10 years of age and 142 (54.0%) patients were >10 years of age. In our study, 48 (36.1%) patients had ALL, 51 (38.3%) patients had AML, 11 (8.3%) patients had HL and 22 (17.3%) patients had NHL and 0.8% had retinoblastoma. In our study, 30 (22.6%) patients had 6-MP, 41 (30.8%) patients had cyclophosphamide, 44 (33.1%) patients had etoposide and 18 (13.5%) patients had methotrexate.

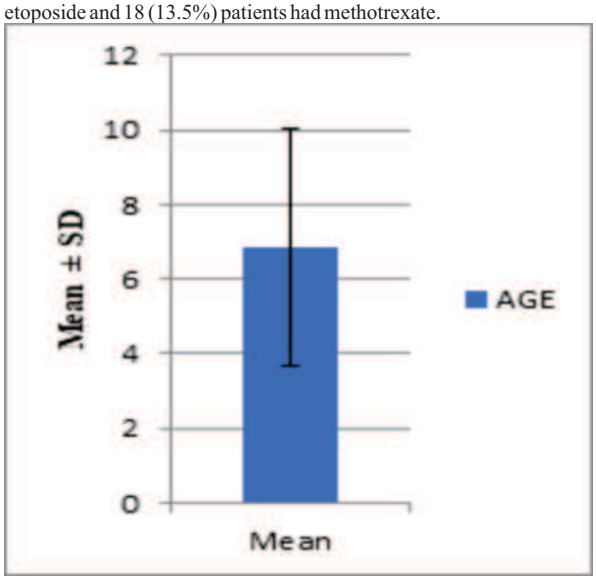

Fig 1: Histogram Showing Age

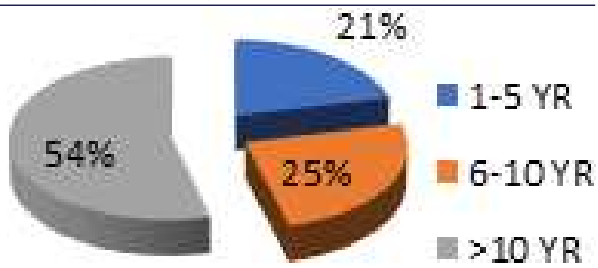

Fig 2: Pie Chart Showing Categorization Of Age

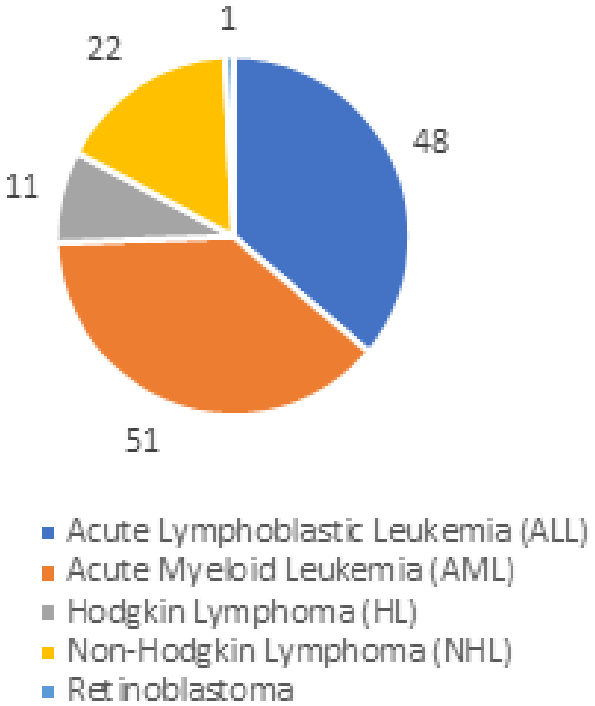

Fig 3: Pie Chart Showing Malignancies In Study Population

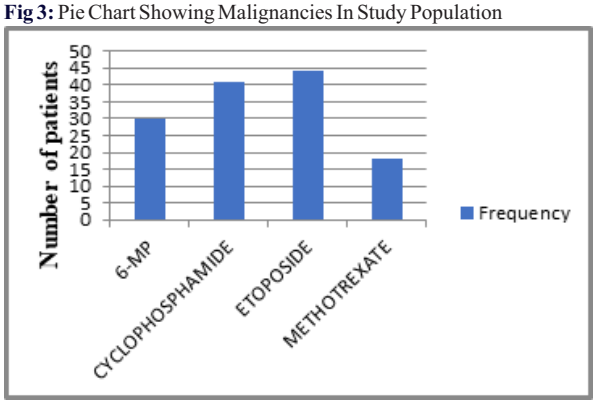

Fig 4: Histogram Showing Percentage Of Metronomic Drugs Distributed Among Study Population

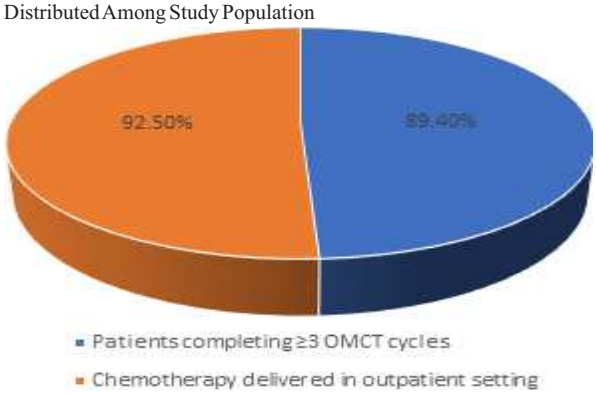

Fig 5. Pie-chart showing Outpatient Feasibility and Treatment Adherence Among Pediatric Patients Receiving OMCT

Treatment Feasibility And Adherence

Feasibility of OMCT was high. A total of 89.4% of patients completed at least three cycles of therapy. Adherence was strong, with 92.5% of chemotherapy delivered in an outpatient setting. Temporary dose interruptions occurred in 9.8% of cases, mostly due to mild reversible toxicities.

DISCUSSION

This prospective study highlights the real-world feasibility and strong outpatient adherence to oral low-dose chemotherapy (OLDC) in pediatric patients with relapsed or refractory malignancies. In a resource-limited tertiary care setting, OLDC was successfully delivered to the majority of patients without the need for hospitalization or intravenous administration, demonstrating its suitability as a decentralized, home-based treatment approach.

The high outpatient feasibility rate (92.5%) observed in our cohort underscores the operational viability of OLDC in pediatric oncology. Unlike conventional intravenous regimens, which require hospitalization, trained personnel, and monitoring infrastructure, OLDC enables treatment in low-acuity settings with minimal clinical supervision. This is particularly advantageous in LMICs, where centralized oncology services are often overwhelmed, and families may face financial or logistical constraints in accessing care.

Treatment adherence was notably high, with nearly 90% of children completing at least three chemotherapy cycles and very few requiring dose interruptions. The low rate of permanent discontinuation (0.8%) and minimal unplanned hospital visits further support OLDC's practicality and tolerability from a systems perspective. These findings align with previous observational reports and pilot trials from LMICs that have proposed OLDC as a feasible option for both palliative care and maintenance therapy in pediatric cancer.

Importantly, caregiver engagement emerged as a cornerstone of successful implementation. High concordance between caregiver-reported adherence logs and physician-verified pill counts (>90%) reflects both the acceptability of OLDC among families and the ease of administration. The absence of significant medication errors or missed visits also suggests that, with proper education, OLDC can be safely managed at home.

Our study contributes critical implementation evidence by assessing not only whether OLDC is safe and effective, but whether it can be reliably delivered outside hospital settings, where conventional care models are not sustainable. As healthcare systems in LMICs shift toward community-based cancer care, evidence from real-world OLDC programs will be essential in shaping policies and protocols that minimize hospital dependence and maximize reach.

However, a few limitations must be noted. This was a single-center study with a relatively short follow-up period of six months. Long-term adherence patterns and barriers were not explored. Additionally, we did not stratify adherence outcomes by caregiver literacy, socioeconomic status, or cancer type, which could inform tailored interventions in the future.

CONCLUSION

This study demonstrates that oral low-dose chemotherapy (OLDC) is a highly feasible and well-adhered-to treatment strategy for pediatric patients with relapsed or refractory malignancies in a resource-limited setting. The majority of patients completed therapy entirely on an outpatient basis, with minimal treatment interruptions and no requirement for hospitalization due to adverse events. High caregiver engagement and reliable follow-up further support OLDC's practicality as a home-based, decentralized cancer care model.

These findings reinforce the role of OLDC as a sustainable and scalable treatment option in low- and middle-income countries, where infrastructure constraints often limit access to standard intravenous chemotherapy. Broader integration of OLDC into pediatric oncology care may help improve treatment continuity, reduce abandonment, and expand access to palliative and maintenance care. Future multicenter and longer-term studies are warranted to validate these findings and guide national implementation strategies.

Conflict Of Interest

The authors declare no conflict of interest related to this study.

Acknowledgement

The authors sincerely thank the Departments of Pharmacology and Oncology, Medical College Kolkata, for their valuable guidance, support throughout the study.

REFERENCES

1. Bhakta N, Force LM, Allemani C, et al. Childhood cancer burden: Global disparities in survival. Lancet Oncol. 2019;20(4): e208–17.
2. Friedrich P, Lam CG, Kaur G, et al. Determinants of treatment abandonment in childhood cancer. Lancet Oncol. 2016;17(9): e478–85.
3. Stefan DC. Patterns of childhood cancer treatment abandonment in Africa. JCO Glob Oncol. 2020; 6:57–65.
4. Ribeiro RC, Pinto CN, et al. Global health system challenges in pediatric oncology. Pediatr Hematol Oncol. 2017;34(5):293–305.
5. André N, Pasquier E, Carré M. Metronomics: shifting paradigms in pediatric chemotherapy. Trends Cancer. 2020;6(10):819–28.
6. Pramanik R, Agarwala S, Gupta YK, et al. Oral chemotherapy vs supportive care in pediatric solid tumors: A randomized trial. JAMA Oncol. 2017;3(9):1222–7.
7. Roberts RD, Wingrove P, et al. Real-world outcomes of low-dose oral chemotherapy in refractory pediatric tumors. Pediatr Blood Cancer. 2024;71(2): e30456.
8. Carcamo B, Francia G. Case series and literature review of oral chemotherapy in pediatric cancers. J Clin Med. 2022;11(10):2849.
9. El-Sayed M, Ali M. Prospective pilot study of OLDC in relapsed pediatric tumors. World J Clin Oncol. 2020;11(4):217–28.
10. Bakhshi S, Arya LS, Jain V, et al. Global OLDC survey in pediatric oncology: Perspectives from LMICs. JCO Glob Oncol. 2019; 5:1–8.
11. Peinemann F, Hoemberg M. OLDC in pediatric extracranial solid tumors: Systematic review. BMJ Open. 2024;14(10): e084477.
12. Sterba J, Valik D, Mudry P. Combined oral chemotherapy for recurrent pediatric cancers. Pediatr Blood Cancer. 2020;67(5): e28279.
13. Fang X, Uno H, Wei LJ. Methodologic approaches for assessing OLDC efficacy. JAMA Oncol. 2018;4(5):743.
14. Bakhshi A, Arya LS. Feasibility of outpatient oral chemotherapy: Indian perspective. Cancer Res Stat Treat. 2022;5(3):45–52.
15. Qayed M, Muscal JA, Ferguson WS, et al. Phase I study of sirolimus with OLDC in children. Pediatr Blood Cancer. 2020;67(4): e28134.
16. Hsu J, Gu W, Brignole M, et al. Health-related quality of life during OLDC in children. BMJ Paediatr Open. 2023;7(1): e001124.
17. Aguilera D, Kim S, Wolff J, et al. Feasibility of outpatient OLDC in CNS pediatric tumors. J Clin Oncol. 2023;41(16_suppl):10024.
18. Carai A, Mastronuzzi A, et al. Home-based chemotherapy: Beyond COVID-19. Pediatr Blood Cancer. 2021;68(10): e29123.