HIGH-DOSE METHOTREXATE (HDMTX) PROTOCOL ADHERENCE: A QUALITY IMPROVEMENT STUDY AT A TERTIARY CANCER CENTER IN PAKISTAN

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INTRODUCTION

High-dose methotrexate (HDMTX) is a integral part of curative therapy for acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma (NHL), and CNS lymphoma. Its narrow therapeutic index and dependence on adequate hydration, urinary alkalinization, and timely leucovorin rescue make strict protocol adherence essential to prevent life-threatening toxicity.

Adherence data from resource-limited, lower-middle-income country settings remain very limited.

AIM

To evaluate adherence to institutional defined protocol an 11-point HDMTX safety check list across 145 infusion cycles, and to determine its association with clinical outcomes — complications, ICU admission, toxic MTX levels, and mortality — in a lower-middle-income country setting.

METHODS

Retrospective quality-improvement review of 145 HDMTX cycles in 68 patients (2024–2025) across 8 chemotherapy protocols at a tertiary cancer center.

An 11 safety points were assessed including pre-/post-MTX hydration, urinary pH monitoring, correct MTX dose & infusion duration, timely leucovorin initiation & dosing, and 24–72-hour MTX clearance.

Outcomes were compared between different groups.

CONCLUSIONS

The 11 safety points HDMTX should be embedded in every hospital HDTMX protocol infusion cycles.

Post-infusion urinary pH monitoring and timely leucovorin rescue are the most critical, modifiable vulnerabilities.

Automated alerts, standardized order sets, and a real-time "Protocol Violation Flag" are recommended to prevent severe toxicity.

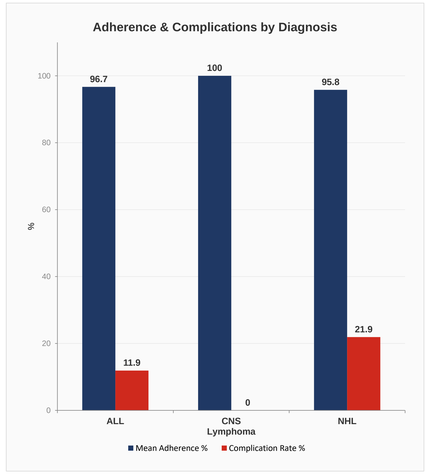
A validated institutional adherence 11 point safety score is proposed for prospective use.

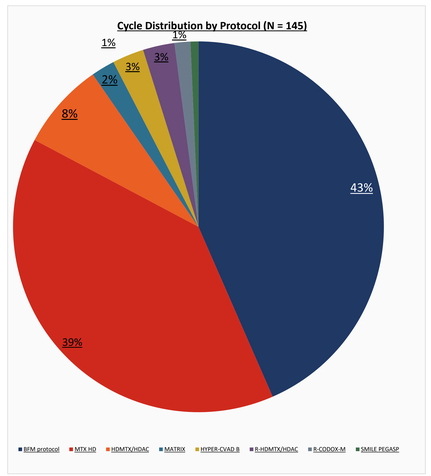
RESULTS

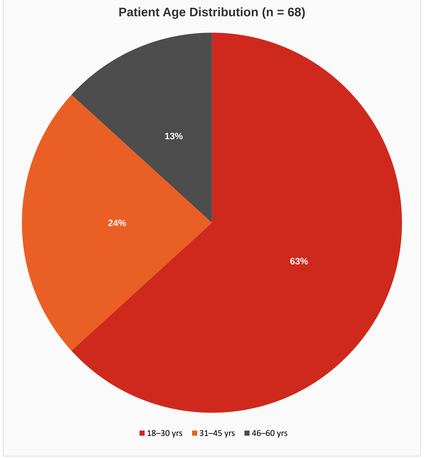
Mean adherence 96.3% — 130/145 cycles (89.7%) achieved >80% adherence. Pre-MTX hydration & urinary alkalinization: 100% compliant. Key gaps: post-MTX urine pH maintenance & leucovorin timing (86.2% each). Toxic MTX levels in 5 cycles (3.4%), all linked to leucovorin dosing/timing errors. Complications in 24 cycles (16.6%); 10 ICU admissions (6.9%), 1 directly MTX-related. <80% adherence cycles had markedly higher complications (40% vs 13.8%), ICU admission (26.7% vs 4.7%), and toxic MTX levels (13.3% vs 2.3%) versus ≥80% adherence cycles.

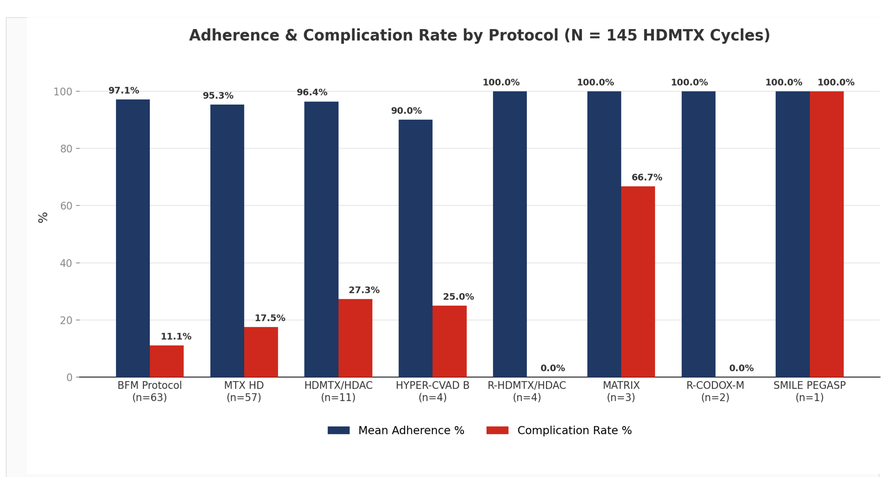
Table 1. Adherence to the 11 Critical HD-MTX Infusion Safety Points (N = 145 cycles)

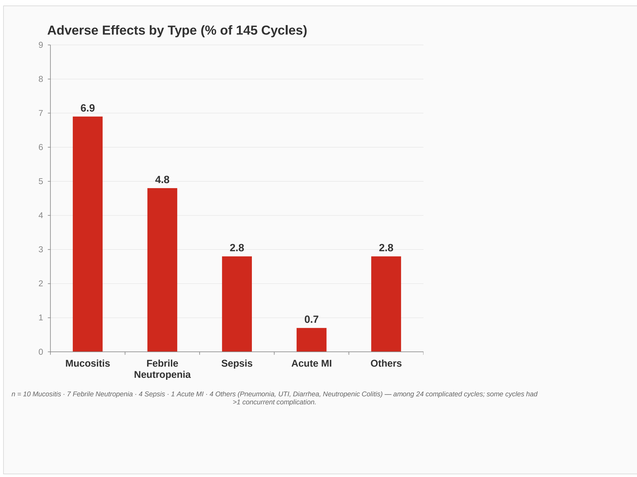
S.No.	Critical Point	Cycles (of 145)	%
1	Pre-MTX Hydration (Correct Rate)	145	100.0%
2	Urine pH ≥8 Achieved ×2 Before Infusion	145	100.0%
3	Baseline Cytopenias	38	26.2%
4	Correct MTX Dose Administered	145	100.0%
5	Correct Infusion Duration Followed	144	99.3%
6	Urine pH Maintained Post-MTX	125	86.2%
7	Leucovorin Given at 24 Hours	125	86.2%
8	Leucovorin Dose & Frequency Correct	138	95.2%
9	Post-MTX Hydration (Correct Rate)	145	100.0%
10	24-Hour MTX Clearance Achieved 48-Hour MTX Clearance Achieved 72-Hour MTX Clearance Achieved	142 143 142	97.9% 98.6% 97.9%
11	Baseline Liver Derangement Dose Reduction Required Contraindicated Drug Used Renal functions Baseline Echo	9 5 1 Normal in 145 cycles Done in 145 cycles	6.2% 3.4% 0.7% - -











n = 10 Mucositis · 7 Febrile Neutropenia · 4 Sepsis · 1 Acute MI · 4 Others (Pneumonia, UTI, Diarrhea, Neutropenic Colitis) — among 24 complicated cycles; some cycles had >1 concurrent complication.

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