IMPACT OF STOOL COLONIZATION WITH MULTI-DRUG RESISTANT BACTERIA IN PATIENTS WITH ACUTE LEUKEMIA RECEIVING INDUCTION CHEMOTHERAPY: A PROSPECTIVE STUDY

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ABSTRACT

AIM

- To assess the prevalence of multi drug resistant (MDR) bacteria in stool cultures of patients with acute leukemia during induction chemotherapy and correlate with the patient outcomes .

METHODS

- It is a prospective study in Acute leukemia patients of 1-60 years of age.
- Stool cultures were collected on day 1 and day 15 during intensive induction chemotherapy.

RESULTS

- The study enrolled 200 patients.
- The median age was 13 years (Range 1- 60 years).
- The major infections were 33(49%) vs 20 (17%) (P value-0.00001) and the induction mortalities were 7(10%) vs 1(1%) (p value 0.0067) in patients of stool cultures with MDR positive vs negative, sent on day 15 of induction chemotherapy respectively.
- Day 1 stool cultures had no correlation with major infections and induction mortalities.

CONCLUSION

- MDR bacteria from day15 stool cultures had strong statistical correlation with major infections and induction mortality, but day 1 stool cultures had no correlation with the same outcomes.

INTRODUCTION

- MDR bacteria are associated with increased morbidity and mortality in patients with acute leukemia (1).
- The present study was conducted to assess the prevalence of MDR bacteria in stool cultures of patients with acute leukemia during induction chemotherapy and correlate with patient outcomes.

METHODS AND MATERIALS

- Newly diagnosed patients with acute lymphoblastic leukemia (ALL) or Acute Myeloid Leukemia (AML) planned for intensive induction chemotherapy were prospectively included in the study.
- Patients age 1 to 60 years were included.
- Stool cultures were collected on day 1 and day 15 of induction.
- Stool culture and sensitivity were done by the routine bacterial culture method using 5% sheep blood agar and Mac conkey agar with Selenite-F broth

RESULTS

- The study enrolled 200 patients between Jan 2018 and March 2020,
- Total 193 patients provided stool samples on day1 and 185 on day 15.
- The median age was 13 years (range 1-60 years),162 (81%) patients had ALL, and 38 (19%) had AML.
- Day 1 stool cultures were positive in 69/193 (35.7%) patients and all grew MDR bacteria. Day 15 stool cultures were positive in 68/185 (36.7%) patients and all grew MDR bacteria (Table 1).
- MDR E.coli and MDR Enterococcus fecium were the most common organisms isolated in the stools (Table 2).
- Positive day 15 stool cultures but not positive day 1 stool cultures were significantly associated with positive blood cultures, mortality, infections, febrile neutropenia, hypoalbuminemia, inotropic support, not attaining remission, and AML (Table 3).
- Day 1 and day 15 stool culture positivity did not significantly correlate with age, sex, nutritional status, diet (neutropenic vs. regular), and induction duration (Table 3).

Table 1: Stool cultures results on day 1 and day 15 of induction chemotherapy

Stool Culture	Day 1 (n=193)	Day 15 (n=185)
Positive	69	68
• Gram Positive	34	24
○ MDR	34	24
○ Non-MDR	0	0
• Gram Negative	34	41
○ MDR	34	41
○ Non-MDR	0	0
• Mixed	1	3
○ MDR	1	3
○ Non-MDR	0	0
Negative	124	117

Abbreviations. MDR: Multi-drug resistant

Table 3: Correlation of day 1 and day 15 stool cultures with demographic and clinical parameters.

Parameter	Day 1 stool culture Positive	Day 1 stool culture Negative	P-Value*	Parameter	Day 15 stool culture positive	Day 15 stool culture Negative	P-Value*
Blood culture Positive Negative	 5 64	 10 114	 0.83	Blood culture Positive Negative	 10 58	 4 113	 0.005
Induction mortality Yes No	 7 62	 7 117	 0.24	Induction mortality Yes No	 7 61	 1 116	 0.002
Infections Yes No	 27 42	 45 79	 0.69	Infections Yes No	 40 28	 31 86	 0.0001
Febrile neutropenia Yes No	 25 44	 43 81	 0.82	Febrile neutropenia Yes No	 40 28	 26 91	 0.0001
Hypoalbuminemia Yes No	 28 41	 52 72	 0.85	Hypoalbuminemia Yes No	 21 47	 57 60	 0.017
Inotropic support Yes No	 13 56	 16 108	 0.26	Inotropic support Yes No	 18 50	 7 110	 0.0001
Post induction complete remission Yes No	 59 10	 109 15	 0.63	Post induction complete remission Yes No	 53 15	 113 4	 0.0001
Use of third-line antibiotics Yes No	 23 46	 24 100	 0.03	Use of third-line antibiotics Yes No	 32 36	 13 104	 0.0001
Age <18 years ≥ 18 years	 50 19	 76 48	 0.11	Age <18 years > 18 years	 45 23	 78 39	 0.94
Sex Male Female	 44 25	 73 51	 0.50	Sex Male Female	 43 25	 72 45	 0.81
Diagnosis ALL AML	 53 16	 102 22	 0.36	Diagnosis ALL AML	 44 24	 106 11	 0.0001
Nutritional status Normal Malnourished	 30 39	 51 73	 0.82	Nutritional status Normal Malnourished	 30 38	 43 74	 0.32
Diet Regular Neutropenic	 40 29	 56 68	 0.88	Diet Regular Neutropenic	 35 33	 56 61	 0.63

Abbreviations. ALL: Acute lymphoblastic leukemia; AML: Acute Myeloid Leukemia. *: Chi-square test.

Table 2. Organisms isolated from stool cultures

Organisms	Day1 stool culture, n=69	Day 15 stool culture, n=68
MDR E.coli	21(30%)	24(35%)
MDR Enterococcus faecalis	10(14%)	5(7%)
MDR Klebsiella pneumonia	12(17%)	17(25%)
MDR Enterococcus faecium	22(32%)	17(25%)
MDR E.Faecium+ MDR.E Coli	1(1%)	3(5%)
MDR Klebsiella + MDR E. Coli	1(1%)	0
VR Enterococcus faecium	2(3%)	2(3%)

Abbreviations. MDR: Multi-drug resistant. VR: Vancomycin-resistant.

DISCUSSION

- MDR stool culture positivity at admission and at Day15 of induction was 36 % in each arm.
- MDR E Coli and MDR Enterococcus fecium were the most common isolated organisms from stool cultures in our study ,which was reported same from other centers in India(2).
- Day 15 stool colonization with MDR bacteria was associated with significant correlation with major infections, febrile neutropenia, septic shock, and induction mortality where as Day1 had no correlation.
- Wells et al study reported that Gram negative bacteria in stool cultures has more risk of bacteremia, infections in neutropenic patients with neutrophils less than 50 cells/mm3(3).
- Vikram et al study reported fecal surveillance cultures had strong correlation with 100 days transplant mortality(4) which supports outcomes in our study.

CONCLUSIONS

Colonization with MDR bacteria in stools on day 15 of acute leukemia induction is associated with an increased incidence of infections, intensive care admissions, and mortality.

REFERENCES

1. Risk factors for mortality in patients with acute leukemia and bloodstream infections in the era of multiresistance, Carolina Garcia-Vidal
2. Infection Prevalence in Adolescents and Adults With Acute Myeloid Leukemia Treated in anIndian Tertiary Care Center Hasmukh Jain, MD, DM
3. Infect control, 1987 Aug; 8(8): The importance of surveillance stool cultures during periods of severe neutropenia, C L Wells 1
4. Multi-Drug Resistant Organisms Are Common in Fecal Surveillance Cultures and Do Not Predict Bacteremia but Correlate with Poorer Outcomes in Patients Undergoing Allogeneic Stem Cell Transplants, Vikram Mathews, MD DM