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MULTI-SITE BACTERIAL COLONIZATION BURDEN AND INFECTION WITH THE CARRIED ORGANISM IN PATIENTS WITH ACUTE LEUKEMIA: A MOROCCAN SINGLE-CENTER RETROSPECTIVE STUDY

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ABSTRACT

Background. Bacterial colonization frequently precedes documented infection in patients with acute leukemia. The prognostic value of multi-site colonization burden remains insufficiently characterized in North African hematology settings. **Objective.** To describe bacterial colonization and infection among leukemia patients in a Moroccan center and to assess the association between the number of positive carriage sites, colonization-infection concordance, and cytopenia depth. **Methods.** We conducted a retrospective single-center study over 2023-2025. Bacteriology records from 97 patients with acute leukemia or related hematological disorders were linked to bone marrow aspirate data using patient identifiers. Specimens were categorized as carriage/colonization or suspected/documented infection. The primary outcome was infection with a carried organism, defined by species-level concordance between a carriage isolate and an infection isolate in the same patient. Trends were assessed using the Cochran-Armitage test. **Results.** Overall, 1,017 bacteriological specimens and 301 isolates were analyzed. Carriage/colonization specimens accounted for 740/1,017 specimens (72.8%), and 292 specimens (28.7%) were bacteriologically positive. Twenty-nine patients (29.9%) carried at least one multidrug-resistant isolate, mostly ESBL-producing bacteria (51/52 MDR isolates). A single carbapenem-resistant Pseudomonas aeruginosa isolate was identified, with no MRSA. Among 32 patients with suspected infection, 17 (53.1%) developed infection with a previously carried species; carriage strictly preceded infection in 11 patients (34.4%). Infection with the carried organism increased with the number of positive carriage sites: 0% for 0 site, 10.0% for 1 site, 21.1% for 2 sites, and 42.9% for >=3 sites (trend p = 0.0013). Rectal and nasal positivity were significantly associated with concordant infection (p = 0.010 and p = 0.008). Concordant infection also increased with cytopenia depth (trend p = 0.046). **Conclusion.** Multi-site bacterial colonization burden was a simple, graded marker of infection risk in leukemia patients. Structured multi-site screening may refine microbiological risk stratification and empirical treatment decisions.

KEYWORDS: acute leukemia; bacterial colonization; multi-site colonization; ESBL; multidrug-resistant bacteria; neutropenia; bone marrow aspirate; concordance.

INTRODUCTION

Patients with acute leukemia are exposed to a major risk of bacterial infection because of disease-related marrow failure, chemotherapy-induced neutropenia, and disruption of mucosal barriers. In this setting, fever may be the only clinical sign of severe infection and warrants prompt broad-spectrum empirical antibiotic therapy.[1,2]

Colonization by multidrug-resistant (MDR) bacteria is now recognized as an important determinant of infectious risk in hematology. Several studies have shown that gastrointestinal or mucocutaneous carriage may precede bloodstream infection or documented infection with the same or a closely related species.[3-8] International recommendations therefore emphasize the integration of local bacterial ecology and previous colonization status into empirical antibiotic selection.[2]

In Morocco, published data on blood cultures and hospital bacterial ecology are available, but studies specifically addressing the colonization-infection continuum in leukemia patients remain scarce. This study aimed to address this gap by linking bacteriological and hematological data from a Moroccan center over a three-year period. The main hypothesis was that carriage extending across several anatomical sites reflects a higher colonization pressure and predicts an increased risk of infection with the carried organism.

MATERIALS AND METHODS

Study design and population. This was a retrospective single-center study conducted in the Laboratory of Medical Biology of Hôpital Universitaire International Cheikh Zaïd, Rabat, Morocco, over the period 2023-2025. Eligible patients had acute leukemia or a related hematological disorder and at least one exploitable bacteriological specimen during the study period.

Hematological data. Diagnostic categories were extracted from bone marrow aspirate reports. Patients were grouped using an operational cytological classification: MPO-positive/probable acute myeloid leukemia (AML), MPO-negative/probable acute lymphoblastic leukemia (ALL), known T-ALL, untyped acute leukemia, or other. The reference complete blood count associated with the bone marrow aspirate was used to compute a composite cytopenia-depth score ranging from 0 to 3, corresponding to the number of affected lineages among hemoglobin <10 g/dL, platelets <150 G/L, and neutrophils <1,500/mm³.

Bacteriological data. Specimens were categorized according to their purpose. Carriage/colonization specimens included screening or usual colonization sites such as rectal, nasal, oral, throat, and swab specimens. Suspected/documented infection specimens included samples collected in a clinical context compatible with infection. Bacterial isolates were recorded by species, microbiological group, and resistance phenotype. MDR isolates were operationally defined as ESBL-producing isolates, MRSA, or isolates showing carbapenem resistance. Methicillin-resistant coagulase-negative staphylococci were described separately and were not counted as MDR according to this operational definition. Because no carbapenemase identification test was performed, the Pseudomonas aeruginosa isolate concerned was reported as carbapenem-resistant and not as carbapenemase-producing.

Outcome definitions. The primary outcome was infection with a carried organism, defined by species-level concordance between a carriage isolate and a suspected/documented infection isolate in the same patient. Three levels of concordance were considered: broad concordance regardless of chronology, previous or concomitant concordance, and strictly previous concordance, in which carriage of the same species was documented before the infection isolate.

Statistical analysis. Categorical variables are expressed as counts and percentages. Proportions were compared using Fisher's exact test. Graded relationships between an ordinal variable and a binary outcome were assessed using the Cochran-Armitage trend test. Statistical significance was set at $p < 0.05$, without adjustment for multiple comparisons; secondary analyses should therefore be interpreted as hypothesis-generating.

Ethical considerations. The data were retrospective and anonymized before analysis. No direct patient identifier is presented in this manuscript.

RESULTS

Cohort characteristics. Ninety-seven patients were included. Sex was available for 94 patients, including 52 women and 42 men. Median age was 39.5 years (range: 4-88 years). MPO-positive/probable AML accounted for 43 patients (44.3%), and MPO-negative/probable ALL for 41 patients (42.3%). Reference neutropenia status included 17 severe, 16 moderate, and 12 mild neutropenia cases; 48 patients were non-neutropenic, and 4 had undetermined status. The cytopenia-depth score was available for 90 patients, including 30 with pancytopenia..

Table 1: General characteristics of the cohort.

Variable	Count	Percentage / value
Patients included	97	100%
Female / male sex	52 / 42	Sex available for 94 patients
Median age	39.5 years	Range: 4-88 years
MPO-positive/probable AML	43	44.3%
MPO-negative/probable ALL	41	42.3%
T-ALL / untyped AL / other	5 / 5 / 3	13.4% overall
Pancytopenia	30/90	33.3% of complete CBCs

Microbiological flow and isolated species. A total of 1,017 bacteriological specimens were analyzed: 740 (72.8%) were classified as carriage/colonization, 270 (26.5%) as suspected or documented infection, and 7 (0.7%) were not classifiable. There were 292 positive specimens (28.7%), corresponding to 301 individualized isolates. The predominant species were Escherichia coli (117 isolates; 38.9%), coagulase-negative staphylococci (65; 21.6%), and Klebsiella pneumoniae (59; 19.6%). Enterobacterales accounted for 182 isolates (60.5%).

Bacterial resistance. Twenty-nine patients (29.9%) carried at least one MDR isolate. The 52 MDR isolates were predominantly ESBL-producing (51 isolates), mainly E. coli and K. pneumoniae. A single carbapenem-resistant Pseudomonas aeruginosa isolate was identified, with no MRSA.

Table 2: Microbiological flow and main resistance phenotypes.

Indicator	Value	Comment
Specimens analyzed	1,017	Period 2023-2025
Carriage/colonization	740 (72.8%)	Specimen purpose
Suspected/documented infection	270 (26.5%)	Specimen purpose
Positive specimens	292 (28.7%)	>=1 bacterium
Bacterial isolates	301	Individualized isolates
MDR isolates	52 (17.3%)	51 ESBL + 1 carbapenem-resistant P. aeruginosa
Patients with >=1 MDR isolate	29/97 (29.9%)	Patient-level analysis
MRSA	0	No isolate identified

Yield by anatomical site. The rectal site had the highest bacteriological yield, with 179/250 positive specimens (71.6%). Yields were lower for other sites, including nasal specimens (52/243; 21.4%) and oral specimens (25/220; 11.4%). Routine urine cultures had a low yield (2/105; 1.9%).

Multi-site burden and infection with the carried organism. The risk of infection with the carried organism increased regularly with the number of positive carriage sites: 0% among patients with no positive site, 10.0% among those with 1 site, 21.1% among those with 2 sites, and 42.9% among those with >=3 sites. The Cochran-Armitage trend test was highly significant (p = 0.0013). Among colonized patients only, the binary comparison of >=2 sites versus 1 site showed an increased risk (26.9% vs 10.0%; OR = 3.32), without reaching statistical significance (p = 0.092).

Table 3. Number of positive carriage sites and risk of infection.

Number of positive sites	n patients	Documented infection (any cause)	Infection with a carried organism
0 site	15	13.3% (2)	0.0% (0)
1 site	30	26.7% (8)	10.0% (3)
2 sites	38	36.8% (14)	21.1% (8)
>=3 sites	14	57.1% (8)	42.9% (6)
Trend	-	p = 0.009	p = 0.0013

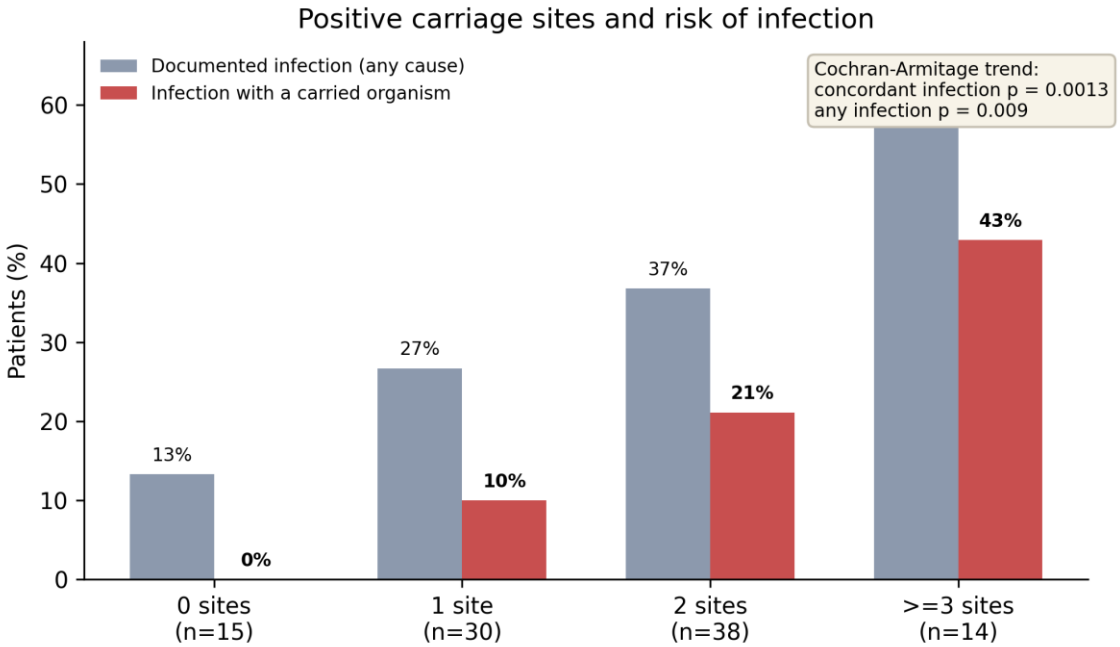

Figure 1. Number of positive carriage sites and risk of infection with the carried organism.

Predictive value of specific sites. All 17 concordant infections occurred in patients with a positive rectal site, whereas none occurred in patients with a negative rectal site (17/75 vs 0/22; p = 0.010). Nasal positivity was also

associated with concordant infection (28.9% vs 7.7%; OR = 4.88; p = 0.008). Oral positivity showed a non-significant trend (28.0% vs 13.9%; p = 0.13).

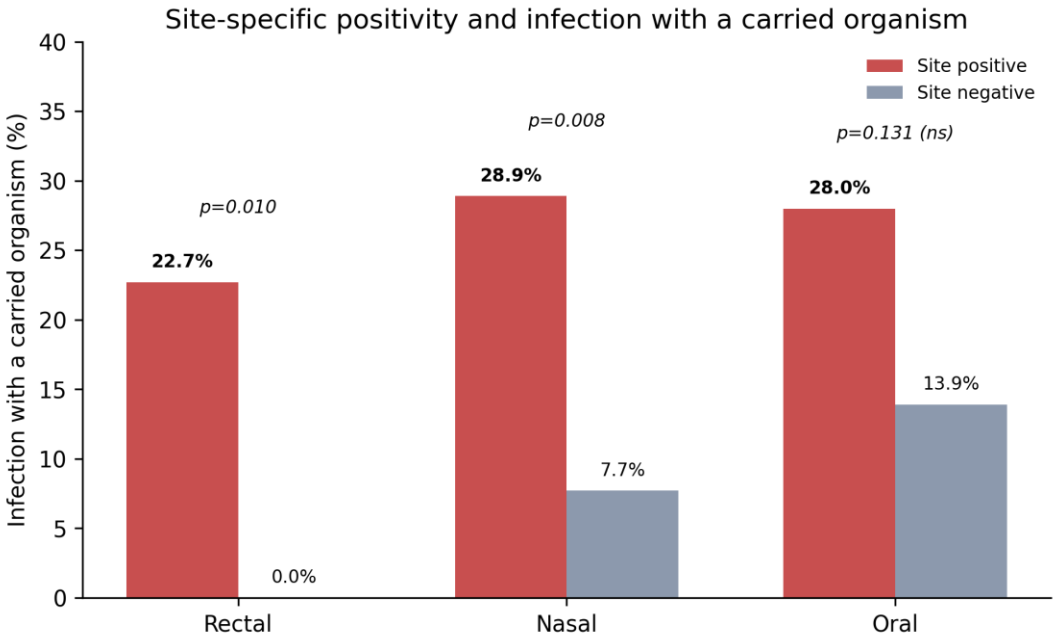

Figure 2: Site-specific positivity and infection with the carried organism.

Colonization-infection concordance and cytopenia depth. Among the 32 patients with at least one suspected/documented infection isolate, species-level concordance was observed in 17 patients (53.1%). Carriage strictly preceded infection in 11 patients (34.4%). Infection with the carried organism was absent in patients with 0-1 affected lineage (0/24) and reached 19.7% in patients with 2-3 affected lineages (13/66; p = 0.017), with a significant trend across the continuous cytopenia score (p = 0.046).

DISCUSSION

This study identifies multi-site colonization burden as a graded marker of the risk of infection with a carried organism in patients with acute leukemia. The main finding was a dose-response relationship between the number of positive anatomical carriage sites and concordant infection, increasing from 0% in the absence of a positive site to 42.9% when three or more sites were colonized. The strength of this relationship, its biological plausibility, and the ease of data collection make it directly relevant to risk stratification.

This signal extends the observations of Torres et al., who showed the value of multi-site screening for anticipating MDR bacteremia in hematology patients.[3] Whereas that study primarily focused on the added yield of multi-site screening for detecting carriage, our study suggests that the anatomical extent of carriage may itself provide prognostic information. Clinically, the number of positive sites could be included in the patient's microbiological summary together with the carried species, resistance phenotype, and neutropenia status.

Species-level concordance between colonization and infection was observed in 53.1% of infected patients, consistent with international studies reporting a link between previous colonization and subsequent infection in hematology patients.[4-8] However, the absence of molecular typing limits interpretation: species-level concordance does not prove clonal identity between the colonizing and infecting isolates. The result should therefore be interpreted as operational microbiological concordance rather than formal proof of endogenous transmission.

The predominance of ESBL-producing organisms among MDR isolates confirms the importance of resistant Enterobacterales in the infectious ecology of leukemia patients. Conversely, documented MDR infections remained uncommon over the study period. This contrast supports the rational use of carbapenems and microbiology-guided de-escalation when the clinical course permits. The Pseudomonas aeruginosa isolate should be reported as carbapenem-resistant in the absence of a specific carbapenemase test, to avoid mechanistic overinterpretation of the phenotype.

The association between cytopenia depth and concordant infection provides an original bridge between marrow cytology and bacteriology. Multi-lineage cytopenia may reflect deeper immunosuppression, longer hospital exposure, and greater vulnerability to bacterial translocation. This observation remains exploratory, as the reference complete blood count does not necessarily reflect the exact hematological status at the time of each bacteriological specimen.

This study has several limitations. Its retrospective design is exposed to selection and sampling-frequency biases: the sickest or longest-hospitalized patients probably underwent more intensive microbiological follow-up. The single-center design limits generalizability. The lack of molecular typing prevents confirmation of strain identity between carriage and infection isolates. Finally, secondary analyses should be considered hypothesis-generating because of the limited sample size and the absence of correction for multiple comparisons.

Despite these limitations, the study has several strengths: the linkage of two biological data sources, patient-by-patient chronological analysis, a substantial number of specimens over three years, and the identification of a simple, graded, clinically interpretable signal. Prospective validation with protocolized multi-site screening, molecular typing of carriage-infection pairs, and adjustment for length of hospitalization would help confirm the predictive value of this approach.

CONCLUSION

In this Moroccan single-center retrospective study, multi-site bacterial colonization burden was strongly and gradually associated with infection with a carried organism in patients with acute leukemia. Rectal positivity captured all concordant infections observed in the cohort, and cytopenia depth was also associated with concordant infection risk. These findings support structured multi-site carriage surveillance and its integration into empirical antibiotic decision-making in hematology units.

Declarations

Conflicts of interest. No conflict of interest.

Data availability. Aggregated data are presented in the article; anonymized individual-level data may be made available upon reasonable request, subject to institutional authorization.

Author contributions. HB: data extraction, statistical analysis, and initial drafting. ZS: data validation, interpretation, and critical revision. RM: data validation, interpretation, and critical revision. AB: scientific supervision, microbiological interpretation, and critical revision.

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