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Article

Predictive Value of Rectal Surveillance Cultures for Bloodstream Infection in Critically Ill Haematological Patients

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Abstract

Background: Bloodstream infections (BSIs) by multidrug-resistant Gram-negative bacteria (MDR-GNB) are associated with high mortality in critically ill haematological patients. Although rectal surveillance cultures (RSC) are increasingly used to detect intestinal colonisation, their ability to predict subsequent BSI remains poorly defined. **Methods:** We conducted a retrospective single-centre cohort study of adults with haematological malignancies admitted to the ICU between January 2020 and December 2024. RSC obtained from seven days before ICU admission until ICU discharge were analysed. We evaluated colonisation dynamics, microbiological concordance between rectal and bloodstream isolates, and the diagnostic performance of RSC for predicting subsequent MDR-GNB BSI. **Results**: Among 400 ICU admissions, 112 (28.0%) patients were colonised at ICU admission and 44 (11.0%) during ICU stay, yielding an overall colonisation prevalence of 39.0%. Admission colonisation was predominantly due to third-generation cephalosporin-resistant Enterobacterales, whereas difficult-to-treat PA was more frequent during ICU stay. Ninety-one BSI episodes occurred, with 67.0% being caused by GNB. Colonised patients developed significantly more GNB BSIs than non-colonised patients (68.9% vs. 31.1%; p = 0.01), and 85.7% of MDR-GNB BSIs were microbiologically concordant with prior RSC. Only one patient with a negative RSC developed subsequent MDR-GNB BSI. The negative predictive value (NPV) of a negative RSC for excluding subsequent MDR-GNB BSI was 99.6% (95% CI 97.7–100%). **Conclusions:** RSC accurately identifies critically ill haematological patients at very low risk of subsequent MDR-GNB BSI. Their high NPV supports their potential role as a decision-support tool for individualising empirical antimicrobial therapy while promoting antimicrobial stewardship.

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Keywords: colonisation surveillance; third-generation cephalosporin-resistant Enterobacterales; carbapenem-resistant Enterobacterales; difficult-to-treat resistance *Pseudomonas aeruginosa*; Gram-negative bloodstream infection; haematological malignancies

1. Introduction

Bloodstream infections (BSIs) caused by multidrug-resistant Gram-negative bacteria (MDR-GNB) are associated with substantial morbidity and mortality in patients with haematological malignancies, especially in those requiring intensive care [1–5]. Because delays in appropriate antimicrobial therapy adversely affect patient outcomes, empirical therapy frequently includes broad-spectrum antibiotics, including carbapenems, novel β-lactam/β-lactamase inhibitor combinations, and combination antibiotic therapy. While this approach increases the likelihood of adequate empirical coverage, it also highlights the challenge of balancing the need for timely and effective therapy against the unintended consequences of unnecessary broad-spectrum antimicrobial use [6].

The gastrointestinal tract is the primary reservoir for MDR-GNB colonisation. Several studies have shown an association between gastrointestinal carriage and subsequent infection, suggesting that colonisation status may help stratify the risk of MDR-GNB BSI and guide empirical antimicrobial therapy [7,8]. However, the predictive value of rectal colonisation for subsequent infection varies across patient populations and epidemiological settings. Patients with haematological malignancies admitted to the intensive care unit (ICU) represent a particularly high-risk population in whom this question is highly relevant [9]. These patients are frequently exposed to prolonged hospitalisation, repeated courses of broad-spectrum antibiotics, invasive procedures and healthcare environments with a high burden of antimicrobial resistance [10,11]. Despite the potential clinical utility of rectal surveillance, data describing the epidemiology of MDR-GNB colonisation and its relationship with subsequent BSI in critically ill haematological patients remain poorly defined.

A better understanding of the predictive value of rectal colonisation surveillance could support more individualised empirical treatment strategies in this setting [12]. Therefore, we aimed to describe the prevalence and dynamics of rectal colonisation in critically ill haematological patients and assess the concordance between colonising and bloodstream isolates to determine the potential clinical utility of rectal surveillance for guiding empirical antimicrobial therapy in this high-risk population.

2. Results

2.1. Study Population and Baseline Characteristics

During the study period, 6.282 hospital admissions among patients with haematological malignancies were recorded. Of these, 400 ICU admissions involving 337 individual patients were identified. Baseline demographic and clinical characteristics are summarised in Table 1.

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Table 1. Baseline characteristics of ICU admissions of haematological patients included in the study.

Characteristics	Total (n = 400)
Demographics	
Female sex	159 (39.8)
Age (years)	62 (49–71)
Comorbidities	
Chronic heart disease	162 (40.5)
Hypertension	112 (28.0)
Chronic pulmonary disease	89 (22.3)
Diabetes mellitus	56 (14.0)
Chronic renal disease	53 (13.3)
Previous solid tumour	46 (11.5)
Recent hospitalisation [1]	
ICU	54 (13.5)
Other wards	162 (40.5)
Recent (<3 months) antibiotic exposure	261 (65.3)
Underlying haematological malignancy	
Lymphoma	
Hodgkin lymphoma	19 (4.8)
Non-Hodgkin lymphoma	166 (41.5)
Acute leukaemia	
Acute myeloid leukaemia	66 (16.5)
Acute lymphoblastic leukaemia	32 (8.0)
Multiple myeloma	43 (10.8)
Chronic myeloproliferative disorder	27 (6.8)
Myelodysplastic syndrome	27 (6.8)
HSCT	
Allogeneic	16 (4.0)
Autologous	68 (17.0)
cGVHD	32 (8.0)
Admission source	
Emergency department	165 (41.2)
Ward	203 (50.8)
Other hospital	32 (8.0)
Severity and organ dysfunction at ICU admission	
APACHE II score	15 (12–18)
SOFA score	5 (3–7)
Organ dysfunction	
Respiratory failure	111 (27.8)
Sepsis/septic shock	89 (22.3)
Cardiovascular failure	12 (3.0)
Neurological dysfunction	51 (12.8)
Renal failure/electrolyte imbalance	13 (3.3)
Hepatic disorders	5 (1.3)
Haemorrhagic complications	17 (4.3)
Monitoring	81 (20.3)
Multiple causes	14 (3.5)
Others	7 (1.8)
Characteristics during ICU stay	
Number of rectal swabs performed	1 (1–2)
Neutropenia during ICU admission	173 (43.3)
Duration of neutropenia, days	4 (2–6)
Organ support	
IMV	85 (21.3)

NIV	32 (8.0)
HFNO	139 (34.8)
Vasopressor therapy	158 (39.5)
CRRT	33 (8.3)
ICU length of stay, days	6 (3–10)
Clinical outcomes	
ICU mortality	72 (18.0)
Mortality at 3 months	152 (38.0)
Mortality at 6 months	202 (50.5)
Mortality at 12 months	260 (65.0)

[1] Hospitalisation >48 h within the previous 3 months. Categorical variables are expressed as n (%) and quantitative variables as median (interquartile range). Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; cGVHD, chronic graft-versus-host disease; CRRT, continuous renal replacement therapy; HSCT, haematopoietic stem cell transplantation; ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; NIV, non-invasive mechanical ventilation; HFNO, high-flow nasal oxygen; SOFA, Sequential Organ Failure Assessment.

2.2. Colonisation Status at ICU Admission

Figure 1 summarises the evolution of rectal swab culture results from 7 days prior to ICU admission until ICU discharge.

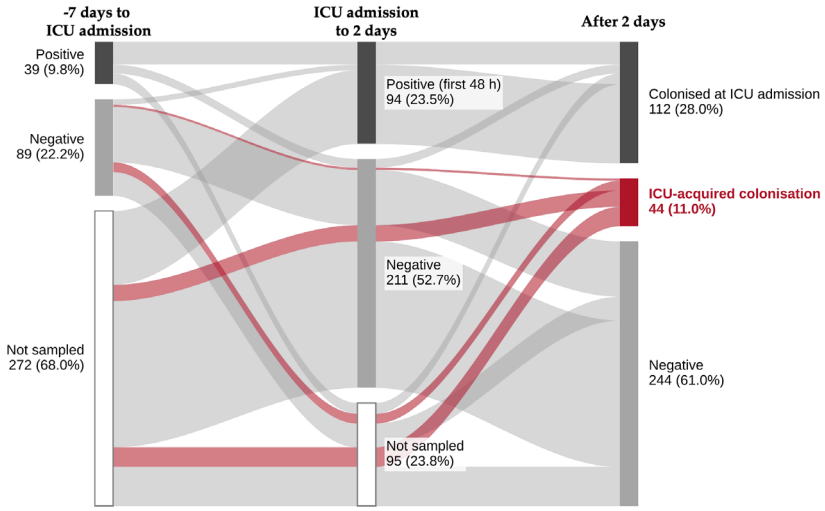


Figure 1. Temporal dynamics of rectal colonisation before and during ICU stay in critically ill haematological patients. Positive/negative cultures of RS were those yielding MDR-GNB. Values are expressed as n (%). The coloured identify the patients colonised in the ICU. Abbreviations: d, days; ICU, intensive care unit; MDR-GNB, Multidrug-resistant Gram-negative bacteria; RS, rectal swab.

During the seven days preceding ICU admission, 139 rectal swabs (RS) were available from 128/400 (32.0%) ICU admissions. Among these admissions, 39/128 (30.5%) had at least one positive RS for MDR-GNB, corresponding to 39 of the 139 RSs performed (28.1%). The median interval between RS collection and ICU admission was 4 days (interquartile range (IQR) 3–5).

Within the first 48 h of ICU admission, 305/400 (76.3%) admissions underwent RS screening, of whom 94/305 (30.8%) had at least one positive RS for the tested microorganisms. Among these, 73/94 (77.7%) represented newly detected colonisation, whereas 21/94 (22.3%) corresponded to previously documented colonisation. Overall, 112/400 patients (28.0%) were considered colonised at ICU admission. The most frequent microorganisms isolated within the 7 days preceding ICU admission and within the first 48 h of ICU admission are detailed in Table S1.

2.3. ICU-Acquired Colonisation

Among the 400 admissions who underwent RS screening during the ICU stay, new colonisation by MDR-GNB was identified in 44 additional patients, accounting for a total of 52 microorganisms. The median time from ICU admission to detection was 8 days (IQR 5–15). The most frequently identified microorganism was *Pseudomonas aeruginosa (PA)* (19/52, 36.5%), of which 5/19 (26.3%) isolates were difficult-to-treat resistant *Pseudomonas aeruginosa* (DTR-PA), followed by *Stenotrophomonas maltophilia* (7/52, 13.5%), *Escherichia coli (E. coli)* (7/52, 13.5%), and *Klebsiella pneumoniae (K. pneumoniae)* complex (7/52, 13.5%). Among Enterobacterales, 17/52 (32.7%) isolates corresponded to third-generation cephalosporin-resistant Enterobacterales (3GCephRE) and 9/52 (17.3%) to carbapenem-resistant Enterobacterales (CRE).

Combining patients colonised at ICU admission (n = 112) with those in whom colonisation was newly detected during ICU stay (n = 44), 156/400 (39.0%) ICU admissions had documented MDR-GNB colonisation. Conversely, 244/400 (61.0%) ICU admissions remained free of detectable MDR-GNB colonisation throughout ICU surveillance (median, 1 RS per admission, IQR 1–2).

During the pre-ICU and intra-ICU colonisation periods, the predominant microorganisms were *E. coli* [56/155 (36.1%) vs. 63/231 (27.3%), p = 0.065], *K. pneumoniae complex* [47/155 (30.3%) vs. 54/231 (23.4%), p = 0.128], and PA [28/155 (18.1%) vs. 36/231 (15.6%); p = 0.521]. Among Enterobacterales isolates, 3GCephRE was the predominant resistance phenotype and was more frequent during the pre-ICU period [93/155 (60.0%) vs. 109/231 (47.2%), p = 0.015], whereas CRE rates were comparable between periods [21/155 (13.5%) vs. 21/231 (9.1%), p = 0.311]. Although the overall prevalence of PA remained stable over time (p = 0.801), DTR-PA was significantly more frequent during the intra-ICU colonisation period [8/155 (5.2%) vs. 36/231 (15.6%), p = 0.002] (Table S2).

The distribution of the most frequently identified microorganisms and their resistance phenotypes during the pre-ICU and intra-ICU colonisation periods is illustrated in Figure 2.

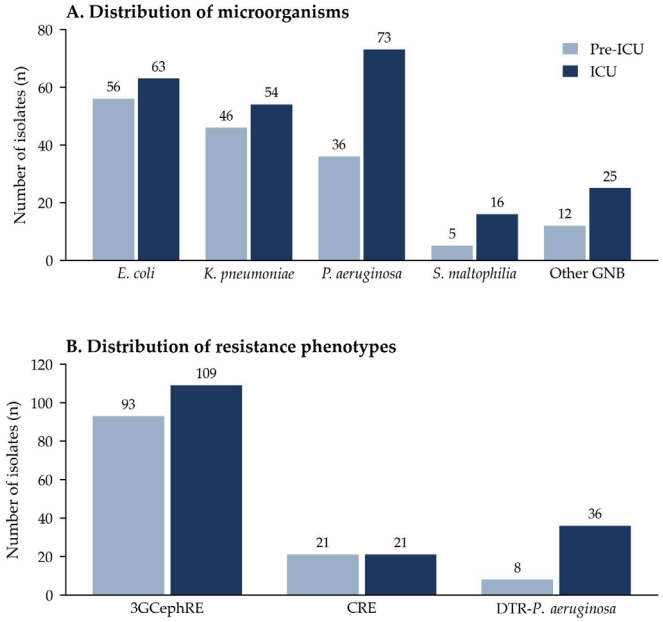


Figure 2. Distribution of microorganisms identified in rectal surveillance cultures before and during ICU stay. Other GNB include *Enterobacter cloacae complex, Citrobacter freundii complex, Citrobacter koseri, and Klebsiella oxytoca/Raoultella ornithynolytica.* Abbreviations**:** 3GCephRE, third-generation cephalosporin-resistant Enterobacterales; CRE, carbapenem-resistant Enterobacterales; DTR, difficult-to-treat resistant; ICU, intensive care unit.

2.4. Bloodstream Infections and Concordance with Prior Rectal Colonisation

A total of 91 BSI episodes were identified in 81/400 (20.3%) ICU admissions. Of these, 46/91 (50.5%) were present on the day of ICU admission, and 45/91 (49.5%) occurred during ICU stay. Overall, 61/91 (67.0%) BSI episodes were caused by GNB (GNB-BSI), of which 29 (47.5%) involved MDR-GNB. The predominant pathogens were *E. coli* (42.6%), *K. pneumoniae complex* (24.6%), and PA (21.3%). Among GNB-BSI episodes, 8/61 (13.1%) were caused by 3GCephRE, 7/61 (11.4%) by CRE, and 2/61 (3.3%) by DTR-PA. The distribution of GNB-BSI episodes according to their temporal relationship with ICU admission is shown in Table S3.

Of the 61 GNB-BSI episodes, 45 (73.8%) occurred in ICU admissions with available surveillance RS data and were therefore evaluable for microbiological concordance analyses. The remaining 16 episodes occurred in admissions without prior RS.

Among the 45 evaluable GNB-BSI episodes, 31 (68.9%) occurred in colonised ICU admissions compared with 14 (31.1%) in non-colonised admissions (p = 0.01). Figure 3 shows the incidence and microbiological concordance of GNB BSI according to prior rectal colonisation status. The median interval from first documented rectal colonisation to BSI was 7 days (IQR 1–10). Of the 31 GNB-BSI episodes occurring in colonised ICU admissions, 21 (67.7%) were caused by MDR-GNB, and 18 (85.7%) were microbiologically concordant with the preceding RS isolate. Three microbiologically discordant episodes were identified: one patient had an RS positive for 3GCephRE and subsequently developed BSI caused by the same microorganism after acquisition of carbapenem resistance; two additional patients had RSs positive for 3GCephRE but developed PA BSI. Only one patient with a negative RS developed an MDR-GNB BSI; this episode was caused by *Stenotrophomona maltophila*, despite a negative surveillance culture obtained 4 days before BSI onset.

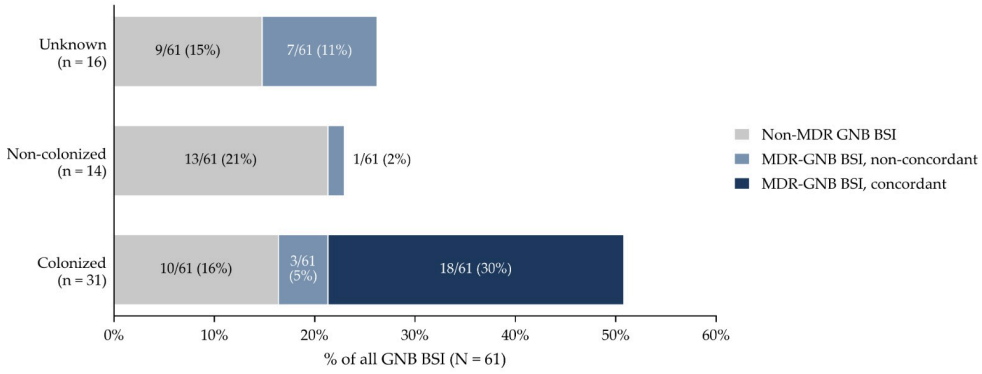


Figure 3. Incidence and microbiological concordance of GNB bloodstream infections (n = 61) according to prior rectal colonisation status. "Unknown" was defined as patients with BSI who had no previous rectal swab available. Abbreviations: BSI, bloodstream infections; GNB, Gram-negative bacilli; MDR-GNB, multidrug-resistant Gram-negative bacteria.

The NPV of a negative rectal swab for excluding subsequent MDR-GNB BSI was 99.6% (95% CI, 97.7–100%). For concordant BSIs, the NPV of rectal surveillance was 100% (95% CI, 98.9–100%) for 3GCephRE, 99.7% (95% CI, 98.5–100%) for CRE, and 99.7% (95% CI, 98.6–100%) for DTR-PA (Table 2).

Table 2. Diagnostic performance of rectal surveillance cultures for predicting concordant MDR-GNB in critically ill haematology patients.

Resistance Phenotype/Microorganism	TP	FP	FN	TN	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	LR+	LR-
ICU admission and throughout ICU stay										
3GCephRE	8	72	0	320	100 (63.1–100)	81.6 (77.4–85.3)	10.0 (4.4–18.8)	100 (98.9–100)	5.4	0.0
Escherichia coli	6	36	0	358	100 (54.1–100)	90.9 (87.6–93.5)	14.3 (5.4–28.5)	100 (99.0–100)	10.9	0.0
Klebsiella pneumoniae complex	2	22	0	376	100 (15.8–100)	94.5 (91.8–96.5)	8.3 (1.0–27.0)	100 (99.0–100)	18.1	0.0
CRE	6	26	1	367	85.7 (42.1–99.6)	93.4 (90.5–95.6)	18.8 (7.2–36.4)	99.7 (98.5–100)	13.0	0.2
Escherichia coli	1	5	0	394	100 (2.5–100)	98.7 (97.1–99.6)	16.7 (0.4–64.1)	100 (99.1–100)	79.8	0.0
Klebsiella pneumoniae complex	4	10	1	385	80.0 (28.4–99.5)	97.5 (95.4–98.8)	28.6 (8.4–58.1)	99.7 (98.6–100)	31.6	0.2
Citrobacter koseri	1	0	0	399	100 (2.5–100)	100 (99.1–100)	100 (2.5–100)	100 (99.1–100)	NE [#]	0.0
P. aeruginosa	2	41	1	356	66.7 (9.4–99.2)	89.7 (86.3–92.5)	4.7 (0.6–15.8)	99.7 (98.4–100)	6.5	0.4
P. aeruginosa DTR	1	13	1	385	50.0 (1.3–98.7)	96.7 (94.5–98.2)	7.1 (0.2–33.9)	99.7 (98.6–100)	15.3	0.5
Stenotrophomonas maltophilia	1	12	1	386	50.0 (1.3–98.7)	97.0 (94.8–98.4)	7.7 (0.2–36.0)	99.7 (98.6–100)	16.6	0.5
During ICU stay										
3GCephRE	4	76	0	320	100 (39.8–100)	80.8 (76.6–84.6)	5.0 (1.4–12.3)	100 (98.9–100)	5.2	0.0
Escherichia coli	3	39	0	358	100 (29.2–100)	90.2 (86.8–92.9)	7.1 (1.5–19.5)	100 (99.0–100)	10.2	0.0
Klebsiella pneumoniae complex	1	23	0	376	100 (2.5–100)	94.2 (91.5–96.3)	4.2 (0.1–21.1)	100 (99.0–100)	17.3	0.0
CRE	3	26	0	371	100 (29.2–100)	93.5 (90.6–95.7)	10.3 (2.2–27.4)	100 (99.0–100)	15.3	0.0
Escherichia coli	1	5	0	394	100 (2.5–100)	98.7 (97.1–99.6)	16.7 (0.4–64.1)	100 (99.1–100)	79.8	0.0
Klebsiella pneumoniae complex	1	13	0	386	100 (2.5–100)	96.7 (94.5–98.3)	7.1 (0.2–33.9)	100 (99.0–100)	30.7	0.0
Citrobacter koseri	1	1	0	398	100 (2.5–100)	99.7 (98.6–100)	50.0 (1.3–98.7)	100 (99.1–100)	399.0	0.0
P. aeruginosa *	2	41	0	357	100 (15.8–100)	89.7 (86.3–92.5)	4.7 (0.6–15.8)	100 (99.0–100)	9.7	0.0
P. aeruginosa DTR	1	13	0	386	100 (2.5–100)	96.7 (94.5–98.3)	7.1 (0.2–33.9)	100 (99.0–100)	30.7	0.0

* Because no specific resistance mechanism is defined for susceptible P. aeruginosa, isolates were classified according to susceptible phenotype only. [#] NE, not estimable because no false-positive results were observed. Diagnostic performance of rectal surveillance cultures for MDR-GNB colonisation to predict concordant BSI during ICU stay was evaluated. True positives (TP) were defined as colonised patients who developed a concordant BSI; false positives (FP) as colonised patients who did not develop a concordant BSI; false negatives (FN) as non-colonised patients who developed a concordant BSI; and true negatives (TN) as non-colonised patients who did not develop a concordant BSI. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) are reported as percentages with 95% confidence intervals (CIs). Positive and negative likelihood ratios (LR+ and LR−) are presented as absolute values. Abbreviations: 3GCephRE, third-generation cephalosporin-resistant Enterobacterales; CRE, carbapenem-resistant Enterobacterales; DTR, difficult-to-treat resistant; GNB-BSI, Gram-negative bloodstream infections; *P. aeruginosa*, *Pseudomonas aeruginosa.*

When the analysis was restricted to the 45 BSI episodes occurring during the ICU stay, 23 (51.1%) were caused by GNB and 10 (22.2%) by MDR-GNB, all of which occurred in previously colonised ICU admissions. No patient with a negative RS developed a concordant MDR-GNB BSI during the ICU stay, resulting in an NPV of 100%.

3. Discussion

This study provides a comprehensive description of the temporal dynamics of rectal colonisation by MDR-GNB in critically ill haematological patients from 7 days before ICU admission until ICU discharge (Figure 1). Four findings deserve particular attention: the high prevalence of colonisation at ICU admission, the frequent acquisition of new colonising microorganisms during the first days of ICU stay, the remarkably high NPV of rectal surveillance for subsequent MDR-GNB BSI, and the high microbiological concordance between RS and BSI isolates.

A substantial proportion of patients were already colonised with MDR-GNB at ICU admission (Table S1), highlighting that colonisation is frequently established before the critical care phase. This observation suggests that routine RS surveillance at ICU admission may provide clinically relevant information to support empirical antimicrobial decisions in this highly vulnerable population. Importantly, the colonisation rates observed in our cohort fall within the range previously reported among haematological and other immunocompromised patients in both conventional wards and ICU settings [8,13]. Current empirical antibiotic strategies are largely guided by epidemiological risk factors for antimicrobial resistance, such as previous antibiotic exposure, recent hospitalisation, or prior colonisation. Our findings suggest that RS surveillance may provide individualised microbiological information that complements these risk-based approaches and may improve empirical antimicrobial selection.

Another relevant observation is that a considerable proportion of initially non-colonised patients acquired colonisation shortly after ICU admission, often within the first week of stay. This finding underscores the dynamic nature of intestinal colonisation in critically ill haematological patients and supports the rationale for serial surveillance during ICU hospitalisation.

Remarkably, the spectrum of colonising microorganisms differed according to the timing of colonisation. Patients colonised at ICU admission were predominantly carriers of ESBL-producing Enterobacterales, whereas those acquiring colonisation during ICU stay more frequently harboured DTR-PA (Figure 2 and Table S2). This temporal pattern may help refine empirical antimicrobial decisions and is consistent with previous observations [8,14]. The finding is biologically plausible and likely reflects differences in the microbial ecology of the environments preceding ICU admission compared with that of the ICU itself. The predominance of ESBL-producing Enterobacterales at admission may be related to prior healthcare exposures and the increasing detection of these organisms in both healthcare settings and the community [15–17]. In contrast, the higher frequency of DTR-PA acquired during ICU stay may reflect the selective pressure exerted by broad-spectrum antimicrobial therapy together with exposure to the ICU environment, where contamination of surfaces and equipment by difficult-to-treat Gram-negative organisms has been widely documented [18,19].

BSIs remain a frequent complication among patients with haematological malignancies and represent both a common reason for ICU admission and a frequent event during an ICU stay, as shown in our cohort [11]. A key finding was the predominance of GNB, which accounted for more than two-thirds of all BSI episodes (Table S3). This proportion exceeds that reported in historical cohorts of haematological patients outside the critical care setting [20], suggesting that Gram-negative pathogens play an even greater role in critically ill haematological patients, as reported in previous cohorts [21–23].

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Colonised patients experienced a significantly higher incidence of BSI than non-colonised patients (Figure 3), consistent with previous observations in haematological populations [24,25]. Several biological mechanisms may underlie this association. Intestinal colonisation by MDR-GNB may reflect profound microbiota disruption characterised by depletion of protective anaerobic commensals and expansion of microorganisms with a high capacity for mucosal translocation [26]. In the critical care setting, sepsis-associated inflammation, hypoperfusion, impaired gastrointestinal motility, and exposure to broad-spectrum antibiotics may further aggravate this dysbiotic state, promoting enrichment of Enterobacterales and *Enterococcus* spp. and increasing susceptibility to both colonisation and bloodstream invasion [27]. Supporting this biological hypothesis, genomic studies have demonstrated that BSIs frequently originate from the patient's own colonising strains [28]. In our cohort, most BSIs occurring in colonised patients were caused by the same microorganism identified in the rectal surveillance cultures. The concordance rate observed was higher than that reported in haematological patients managed outside the ICU [8,29] and comparable to the highest rates described in critical care cohorts [30]. The high microbiological concordance suggests that colonising microorganisms may be the source of most BSIs in colonised patients. However, as reflected by the low PPVs (Table 2), only a minority of colonised patients developed a subsequent concordant BSI. A positive rectal surveillance culture may therefore help anticipate the causative microorganism if BSI develops, while providing limited information on the likelihood of progression to invasive infection. This progression is multifactorial, involving host-, colonisation-, and healthcare-related factors, including the density of intestinal colonisation, which could not be assessed using our qualitative surveillance cultures [7,12].

The most clinically relevant finding of our study was the high NPV of rectal surveillance for ruling out subsequent MDR GNB BSI (Table 2). These results are consistent with previous studies conducted in haematological patients admitted to conventional wards [8,31]. To our knowledge, this is the first study specifically evaluating the diagnostic performance of rectal surveillance cultures in critically ill haematological patients. The absence of rectal colonisation identified a population at very low risk of subsequent MDR-GNB BSI, suggesting that surveillance cultures could facilitate a more individualised approach to empirical antimicrobial therapy, guiding the use of carbapenems, novel β-lactam/β-lactamase inhibitor combinations, and anti-pseudomonal agents. Such a strategy could reduce unnecessary exposure to broad-spectrum antibiotics, thereby preserving the gut microbiota and decreasing the selective pressure that promotes the emergence and spread of antimicrobial resistance [32,33]. Prospective validation is now required to determine whether surveillance-guided empirical therapy is safe and improves antimicrobial stewardship outcomes.

The main strengths of this study include the detailed characterisation of colonisation dynamics and the evaluation of the predictive performance of rectal surveillance for subsequent BSI in a population for whom evidence remains scarce. Several limitations should also be acknowledged. First, the retrospective single-centre design may limit the generalisability of our findings. Local epidemiology, antimicrobial stewardship practices, and infection-control policies are likely to influence the predictive performance of surveillance cultures. Second, not all patients had RS available before BSI onset, largely because a substantial proportion of ICU admissions originated from the Emergency Department or were transferred from other hospitals, where routine surveillance was not systematically performed. Third, implementation of an RS surveillance-guided empirical antimicrobial strategy would require surveillance cultures to detect not only MDR organisms but also susceptible PA. As many rectal surveillance programmes currently focus exclusively on MDR organisms, adaptation of microbiological workflows may be required. Fourth, rectal colonisation and bloodstream isolates were assumed to represent the same strain when

both the microorganism and resistance mechanism coincided; however, strain-level characterisation would be required to confirm their genetic relatedness. Fifth, rectal surveillance cultures were qualitative and provided no measure of colonisation burden. If patients with a lower burden are less likely to develop microbiologically concordant BSI, classifying all colonised patients as culture-positive may partly explain the high number of false positives. Also, the relatively small number of MDR-GNB BSI events may limit the precision of some diagnostic performance estimates. Finally, BSI sources were not systematically documented, precluding estimation of the proportion of episodes of endogenous origin.

4. Materials and Methods

4.1. Study Design and Setting

This retrospective observational cohort study was conducted at Hospital Clínic Barcelona, a tertiary-care university hospital with a dedicated Haematology Department. The study setting was the 13-bed medical ICU, the referral unit for critically ill haematological patients. The study period extended from January 2020 to December 2024. Reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

4.2. Study Population

All consecutive adult patients (≥18 years) with haematological malignancies admitted to the ICU who underwent at least one surveillance rectal swab during their ICU stay were included. For patients with multiple ICU admissions during the study period, each admission was analysed as an independent episode.

4.3. Institutional Surveillance Protocol

RS screening for MDR-GNB in the ICU and haematology wards was recommended as part of a structured institutional infection-control programme at admission and on a weekly basis. The decision to perform RS screening was made by the treating physician for each patient, without any direct intervention by the study investigators.

The surveillance programme targeted 3GCephRE, including extended-spectrum β-lactamase (ESBL)-producing and AmpC-hyperproducing; CRE; PA (with subsequent classification as susceptible or DTR strains); and other resistant non-fermenting GNB. Multidrug-resistance phenotypes were classified according to the European Society of Clinical Microbiology and Infectious Diseases consensus definitions [34]. Blood cultures were obtained during all febrile episodes and repeated based on clinical judgement. According to institutional protocol, fluoroquinolone prophylaxis was administered to patients with anticipated prolonged neutropenia (absolute neutrophil count $<0.5 \times 10^9$/L for >10 days).

4.4. Data Collection

Potentially eligible episodes were identified through a structured query of the institutional electronic health records, selecting all ICU admissions of patients hospitalised under the Haematology Department, together with their corresponding microbiological and clinical data. All episodes were subsequently reviewed manually by three investigators (J.C.-G, A.G.-P., A.B.C.) to verify inclusion criteria.

Collected data included baseline demographics, comorbidities, recent hospitalisation and antibiotic exposure, haematological diagnosis, transplant history, severity at ICU admission (Acute Physiology and Chronic Health Evaluation II [APACHE II] [35] and Sequential Organ Failure Assessment [SOFA] [36]), organ support requirements (invasive

mechanical ventilation (IMV), non-invasive mechanical ventilation (NIV), high-flow nasal oxygen (HFNO), vasoactive drugs, and continuous renal replacement therapy), neutropenia duration, and all RS and blood culture results obtained throughout the index hospitalisation. Patients were followed for one year after ICU admission or until death; vital status was ascertained from electronic health records, and all-cause mortality was assessed at ICU discharge and at 3, 6, and 12 months after ICU admission.

4.5. Definitions

An RS was considered positive when any of the surveillance-targeted organisms were isolated. Colonisation was defined as at least one positive RS. A patient was classified as colonised from the date of the first positive RS and remained so until decolonisation criteria (three consecutive negative RSs) were met.

The pre-ICU colonisation period was defined as the 7 days preceding ICU admission plus the first 48 h after ICU admission. Patients were considered colonised on ICU admission if at least one RS obtained during this period was positive. The intra-ICU colonisation period was defined as the period starting >48 h after ICU admission. ICU-acquired colonisation was defined as a first positive RS obtained >48 h after ICU admission in patients without documented colonisation during the pre-ICU period.

Bloodstream infection was defined as the isolation of a recognised pathogen from at least one blood culture set, or the isolation of common skin commensals (coagulase-negative staphylococci, *Corynebacterium* spp.) from at least two independent sets. Persistent BSI was defined as continued positive blood cultures for the same microorganism despite appropriate antimicrobial therapy. Only the index episode of persistent BSI was included in the analysis. According to their temporal relationship with ICU, BSI episodes were categorised as bacteraemia at ICU admission or ICU-acquired bacteraemia. A BSI was classified as concordant when the same species harbouring the same resistance mechanism was identified in both the blood culture isolate and a preceding RS isolate obtained within the previous week. Patients without an RS obtained before the date of BSI onset were excluded from the analysis of microbiological concordance.

4.6. Microbiology

RS were inoculated onto chromID ESBL agar for detection of extended-spectrum cephalosporin-resistant Enterobacterales and chromID CARBA SMART agar for detection of carbapenem-resistant organisms (bioMérieux, Marcy-l'Étoile, France). Blood cultures were processed using the BACTEC FX continuous-monitoring system (Becton Dickinson, Franklin Lakes, NJ, USA). In both settings, species identification was performed by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Bremen, Germany), and antimicrobial susceptibility was determined by disc diffusion and automated broth microdilution (BD Phoenix system; Becton Dickinson). ESBL production was confirmed by double-disc synergy testing with cefotaxime, ceftazidime, and cefepime discs placed adjacent to a clavulanic acid disc. AmpC hyperproduction was suspected in cefoxitin-resistant isolates and confirmed by boronic acid disc testing. Carbapenemase production was screened by lateral-flow immunochromatography (NG-Test CARBA 5; NG Biotech, Guipry, France); carbapenem-resistant isolates yielding a negative immunoassay were further evaluated by the modified carbapenem inactivation method. All results were interpreted according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints [37].

4.7. Statistical Analysis

Continuous variables were reported as median with IQR and compared using the Mann–Whitney U test. Categorical variables were expressed as counts with percentages

and compared using the chi-squared or Fisher's exact test as appropriate. The diagnostic performance of RS for predicting subsequent concordant MDR-GNB BSI was evaluated by calculating sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios with exact 95% confidence intervals. Performance metrics were computed for the intra-ICU period, and separately for each resistance phenotype. A two-sided p-value < 0.05 was considered statistically significant. Data extraction and preprocessing were performed using Python (version 3.14; Python Software Foundation) and Dataiku (version 14; Dataiku Inc., New York, NY, USA). Statistical analyses were conducted using R version 4.5 (R Foundation for Statistical Computing, Vienna, Austria) within the RStudio integrated development environment (Posit Software, PBC, Boston, MA, USA).

5. Conclusions

RS surveillance cultures provide clinically relevant patient-specific microbiological information that may help identify critically ill haematological patients at risk of subsequent MDR-GNB BSI. Their high NPV suggests a potential role in supporting more individualised empirical antimicrobial therapy and optimising the use of broad-spectrum antibiotics. However, prospective multicentre studies are warranted to evaluate the clinical benefit, safety, and ecological impact of implementing surveillance-guided empirical antimicrobial strategies in routine clinical practice.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/antibiotics15121185/s1: Table T1: Epidemiology of rectal swab cultures at ICU admission; Table T2: Rectal swab isolates of MDR-GNB and their associated resistance mechanisms according to the study periods; Table T3: Distribution of GNB-BSI episodes stratified by ICU period.

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Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request due to privacy and confidentiality considerations.

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Abbreviations

The following abbreviations are used in this manuscript:

3GCephRE	Third-generation cephalosporin-resistant Enterobacterales
APACHE II	Acute Physiology and Chronic Health Evaluation II
AmpC	AmpC β-lactamase
BSI	Bloodstream infection
CRE	Carbapenem-resistant Enterobacterales
DTR	Difficult-to-treat resistance
ESBL	Extended-spectrum β-lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GNB	Gram-negative bacteria
HFNO	High-flow nasal oxygen
ICU	Intensive care unit
IMV	Invasive mechanical ventilation
IQR	Interquartile range
MALDI-TOF MS	Matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry
MDR-GNB	Multidrug-resistant Gram-negative bacteria
NIV	Non-invasive ventilation
NPV	Negative predictive value
PA	*Pseudomonas aeruginosa*
PPV	Positive predictive value
RS	Rectal swab
SOFA	Sequential Organ Failure Assessment
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

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