Abstract Highlights

The following selected highlights spotlight several interesting and timely abstracts presented at the 2023 European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) congress, covering topics such as subacute and chronic meningitis diagnosis, multidisciplinary approaches for *Clostridioides difficile* treatment, and bloodstream infection risk factors.

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Risk Factors for Gram-negative Bloodstream Infection Revealed

FOLLOW-UP blood cultures (FUBC) are controversial; while positive FUBCs are an effective prognostic marker associated with increased survival, they are also associated with longer hospital stays and increased treatment duration.

Researchers at the Infectious Diseases Unit and the Clinical Pharmacology Unit, IRCCS Azienda Ospedaliero Universitaria di Bologna, Italy, conducted a systematic review and meta-analysis to assess the impact of FUBCs on the outcome and management of patients with Gram-negative bloodstream infection (GN-BSI) along with the risk factors for persistent GN-BSI. PubMed-MEDLINE, Scopus, and Cochrane Library Database were independently searched until 24th June 2022 to retrieve randomised control trials and observational studies. Studies were excluded if quantitative target outcome results for intervention or comparator group were missing, or if data adjusted for cofounders was unavailable. Data was extracted and the quality of each included paper was assessed according to the risk of bias 2 tool for randomised control trials, and ROBINS-1 tool for observational studies. The meta-analysis was then performed by pooling adjusted odds ratios (OR) using a random-effect model with inverse variance method.

The database search identified 3,747 articles, which were screened, resulting in the identification of 11 studies. Overall, the execution of FUBCs was associated with a significantly lower risk of mortality (OR: 0.58; 95% confidence interval [CI]: 0.49–0.70) without heterogeneity ($p=0.68$; $I^2=0.0\%$) and publication bias. However, FUBCs were also associated with increased treatment duration (standardised mean difference: 0.65; 95% CI: 0.45–0.84) and longer hospitalisation (standardised mean difference: 0.75; 95% CI: 0.19–1.31). Regarding independent risk factors for a positive FUBCs, end-stage renal disease (N=3; OR: 2.99; 95% CI: 1.77–5.05), central venous catheters (N=4; OR: 3.30; 95% CI: 1.82–5.95); infections due to extended spectrum β-lactamase or carbapenemase-producing *Enterobacteriaceae* (N=4; OR: 3.24; 95% CI: 2.01–5.23); resistance to empirical treatment (N=3; OR: 2.70; 95% CI: 1.65–4.41); and an unfavourable response within 48 hours (N=2; OR: 2.99; 95% CI: 1.44–6.24) emerged. No substantial heterogeneity or publication bias were found.

Overall, the analysis could aid with the stratification of patients at low or high risk for persistent bacteraemia, thus optimising the use of FUBCs in patients with GN-BSI.

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Multidisciplinary Review and Diagnostic Approaches Align for the Treatment of *Clostridioides Difficile*

A RECENT prospective, multidisciplinary review has recognised the value that comes with the alignment of multidisciplinary review and diagnostic approaches in the treatment of *Clostridioides difficile* infection (CDI).

Researchers from Beaumont Hospital, Dublin, Republic of Ireland, and the Royal College of Surgeons in Ireland (RCSI) ran a retrospective study to assess the current two-step testing guideline approach for clinicians to diagnose CDI. At Beaumont Hospital, the testing protocol was amended in 2015, first using a PCR test to check for *C. difficile*, and following this with an enzyme immunoassay (EIA) to check for *C. difficile* toxin if the PCR test indicated a positive result.

The impacts of this approach, as well as surveillance categories and treatment for CDI infection, were reviewed using data from between 2016–2021 held in a centralised database. Data included laboratory results for *C. difficile*, treatment details, case category, and origin of cases. Every positive PCR result was given a weekly prospective, multidisciplinary review.

Researchers created three categories for cases of CDI: case definition criteria fulfilled; case definition unmet, but clinical treatment for CDI indicated; and case not meeting definitions, with no treatment necessity. Sensitivity and specificity analyses determined CDI from positive EIA toxin results. Researchers also utilised χ^2 analyses in order to investigate possible associations existing between the case definition and EIA toxin results.

Data included 1,305 PCR results positive for *C. difficile*. Of these, 43.1% were positive for EIA toxin and 56.9% negative. Around one-third of results failed to meet case definition, and no treatment was therefore needed; 59.2% of results were positive for CDI; and 6.7% of cases did not meet definition, but treatment was clinically indicated. Of those requiring treatment, 43.0% were toxin-negative. Toxin-positive patients were more likely to meet the case definition for CDI (odds ratio: 4.6; $p<0.01$; 95% confidence interval: 3.6–6.0).

Researchers concluded that when clinicians are diagnosing CDI, it is important not to depend on the results of a single laboratory test. Using a multidisciplinary approach is optimal for patient management, as well as diagnosing definite cases of CDI.

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What Increases 30-Day Mortality Risk in Bloodstream Infections?

WORLDWIDE incidence of vancomycin-resistant enterococci is increasing. Therefore, researchers from the Trieste University Hospital, Italy, investigated enterococcal blood stream infections risk factors and 30-day mortality, focusing on *Enterococcus* species, vancomycin resistance, and appropriate treatment. The team also investigated if the timing of receiving appropriate treatment had an impact on 30-day mortality.

Most cases of nosocomial bloodstream infections are caused by *Enterococcus faecalis* and *Enterococcus faecium*. All patients aged >18 years who had a positive blood culture of either were retrospectively included in this study. Appropriate antibiotic therapy was defined as active therapy against isolated *Enterococcus* commencing within 24 hours of diagnosis, and lasting for a minimum of 5 days.

Of the 584 patients included in this study, 93 had vancomycin-resistant *E. faecium*. The 30-day mortality was analysed with a multivariable Cox model. The 30-day mortality rate for vancomycin-resistant *E. faecium* bacteraemia was higher when compared to vancomycin-sensitive *E. faecium* and vancomycin-sensitive *E. faecalis* (hazard ratio [HR]: 1.701; 95% confidence interval [CI]: 1.214–2.383; p=0.002). However, male gender and an infectious disease consultation were independently associated with lower mortality (HR: 0.666; 95% CI: 0.481–0.921; p=0.014; and HR: 0.504; 95% CI: 0.352–0.719; p<0.001, respectively).

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Further, the mortality rate was 11.4% when antimicrobial treatment commenced within 24 hours; however, this rose when active therapy started later. Appropriate antimicrobial treatment was also associated with lower mortality (HR: 0.682; 95% CI: 0.488–0.955; p=0.026). However, Pitt bacteremia score (PBS) and complicated bacteremia are independently associated with higher mortality (HR: 1.269; 95% CI: 1.192–1.350; p<0.001; and HR: 1.818; 95% CI: 1.304–2.535; p<0.001, respectively).

Delayed antimicrobial treatment is associated with a higher 30-day mortality rate, and there is a higher risk of 30-day mortality with vancomycin-resistant *E. faecium* bacteraemia.

Aetiologic Diagnosis of Subacute and Chronic Meningitis Remains Challenging

NEW research confirms the challenges in diagnosing the aetiology of subacute or chronic meningitis (SOCM). While diagnostic tests to identify causes of SOCM have expanded, with metagenomic next-generation sequencing to aid the identification of novel or unexpected pathogens, these techniques are expensive and not always accessible, especially in low- or middle-income countries.

A team reviewed medical records and discharge letters of patients 16 years and older (median age: 37 years) with SOCM who were admitted between March 2015–September 2019 in Mashhad, Iran, as well as online patient registration forms of those admitted between October 2019–October 2022. They scored outcomes using the Glasgow Outcome Scale (GOS).

In total, 183 episodes of SOCM were diagnosed. The most common infectious cause of SOCM was tuberculous meningitis, with 86 (47%) cases, followed by Brucella meningitis with 45 (24.6%) cases. In 72 (39.3%) cases, aetiology was confirmed; however, it remained unknown in 45 (24.6%) and presumptive in 66 (36.1%). Mortality rate before hospital discharge was 14.3%, but 44 (29.3%) patients who survived experienced unfavourable outcomes. Of note, patients with an unknown aetiology were at higher risk of in-hospital death compared with those with proven or presumptive diagnosis (31.1% versus 8.7%; p<0.001; odds ratio: 4.74; 95% confidence interval: 1.996–11.267).

The team concluded that determining the cause of SOCM remains a challenge, as less than 40% of episodes led to a cause-specific diagnosis. Approximately half of the patients experienced unfavourable outcomes, and those with an unknown cause had a five-times higher risk of in-hospital death. Therefore, more efforts to find the causes of SOCM are necessary to improve patient outcomes, and more rapid, accurate, and low-cost tests are necessary for this.

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