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Escherichia coli bacteraemias in intensive care unit patients

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Abstract

Background: Although bacterial infections are common in critically ill patients, isolation of bacteria from the sample is not always unambiguous.

The authors addressed *Escherichia coli* bacteraemia in patients treated in the Intensive Care Unit in the Teaching Hospital in Gdansk in 2002–2009.

Methods: Using a computer database, the names of *Escherichia coli* positive patients and dates of blood sampling were found, followed by a retrospective assessment whether positive blood cultures were accompanied by the clinical features of sepsis or asymptomatic bacteraemia.

Results: Positive cultures were found in 40 blood samples (36 patients). Bacteraemia was diagnosed in 11, sepsis in 10, severe sepsis in 6 and septic shock in 13 cases. In the bacteraemia group, the condition originated from the gastrointestinal tract — 4 cases; from the lungs — 1; while in 6 cases, the aetiology was not detected. In patients with an infection, the likely source was the gastrointestinal tract — 12 cases; the lungs — 4; and pyothorax — 2. In 11 cases, the aetiology remained unidentified. In 3 patients in the bacteraemia group, cultures of other microorganisms were found to be positive, while there were 4 cases among the septic patients. In the bacteraemia group, 8 patients died in the intensive care unit, without relation to bacteraemia. Amongst septic patients 17 died, including 12 whose death was probably attributable to *Escherichia coli* infection.

Conclusions: *Escherichia coli* bacteraemias and infections have been and will remain an everyday problem in hospital wards. The differentiation of asymptomatic bacteraemia from infection is essential for rational antibiotic therapy, which is particularly important considering the increasing resistance of microorganisms.

Key words: bacteraemia, blood stream infection, *Escherichia coli*, intensive care unit

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The isolation of a pathogen from a patient's blood should be alarming for a clinician. However, pathogen isolation from the bloodstream does not necessarily mean an infection. When the clinical features of infection are absent, bacteraemia is diagnosed. Before such a diagnosis is established, the clinical condition of the patient should be meticulously analysed and the possible features of infection carefully sought in order to avoid overlooking anything relevant.

The most commonly reported factors responsible for blood infections are Gram (+) bacteria, which is associated with permanent vascular catheters, temporary vessel cannulation or widely applied invasive procedures. On the other hand, Gram (–) pathogens are commonly isolated in specimens from critically ill patients.

The available data regarding *Escherichia coli* (*E. coli)* bacteraemia and sepsis in Poland are limited.

During the period 2001–2003, *E. coli* bacteraemia cases observed in the Teaching Hospital in Gdansk accounted for 7% of all the bacteraemia cases diagnosed during this period [1].

The authors of the present study addressed *E. coli* bacteraemia and sepsis in patients treated in the Intensive Care Unit in an attempt to analyse the issue in detail.

METHODS

The study's design was approved by the Independent Bioethics Committee for Research Studies attached to the Medical University of Gdansk. Since the study was retrospective, and based on database information and medical records of patients, their informed consent was not required.

Initially, the study encompassed 38 patients treated in the Department of Intensive Care, in the Teaching Centre of the Medical University of Gdansk during the period 2002–2009.

Using the database of the Department of Clinical Microbiology, the names of *E. coli* positive patients and the dates of blood sampling were generated. Subsequently, the clinical data from their medical histories were analysed.

Based on the information obtained, we retrospectively assessed whether positive blood cultures were accompanied by clinical features of infection or asymptomatic bacteraemia.

To determine whether positive blood cultures were accompanied by the symptoms of sepsis, severe sepsis or septic shock, the criteria included in the international guidelines "Surviving Sepsis Campaign 2012" for management of severe sepsis and septic shock [2] were used, and which are recommended by the National Consultant for departments of anaesthesiology and intensive care in Poland [3].

Venous blood cultures taken from hospitalized patients were ordered by a doctor due to a suspicion of bacteremia and/or septicemia. The blood cultures were taken following standard procedures using a transporter-multiplying medium with an antibiotic inactivator and/or chemotherapeutic drug inactivator (activated charcoal) allowing for optimal conditions for the growth of aerobic and anaerobic bacteria (BacT/ALERT SA AerobicBacT/ALERT SN Anaerobic, BacT/ALERT FAN Aerobic, BacT/ALERT FAN Anaerobic.). Blood samples were incubated up to 7 days using the automatic Bact/Alet system (bioMerieux). In patients with suspected fungal or gram negative microbial infections from HACEK groups (Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens and Kingella kingae), the blood cultures were incubated between 14 and 21 days.

The positive blood cultures which were analysed using gram staining, microscopic examination of cell morphology, while cell walls were inoculated on a stable multiplying medium (Columbia Agar with a 5% addition of sheep blood provided by bioMerieux) and a selective-isolating medium (MacConkey Agar, Columbia CAN Agar with a 5% addition of sheep's blood, chocolate agar with an addition of PolyViteX, Sabouraud Agar with gentamicin and chloramphenicol 2, bioMerieux) were performed according to standard procedures. Simultaneously, from the positive blood culture (125 μL), an antibiogram was performed *in cito* using the disk-diffusing Kirby Bauer method (Mueller Hinton 2 Agar or Mueller Hinton Agar with a 5% addition of sheep blood, bioMerieux)

Table 1. The incidence of bacteraemia or infection in positive blood cultures

	Bacteraemia	Sepsis	Severe sepsis	Septic shock
Number (%) of positive blood cultures	11 (27.5)	10 (25)	6 (15)	13 (32.5)

RESULTS

During the study period, *E. coli* bacteria were cultured in 42 blood samples. In one case, the date of the culture did not coincide with the patient's stay in the unit and the patient was excluded from further analysis. Moreover, a patient whose medical records were not found was also excluded. In four patients, *E. coli* was cultured twice during the ICU stay at the interval of 2, 4, 6 and 18 days. One of them had been treated twice in the ICU — in 2004 and 2008 — during both hospitalisations *E. coli* cultures were positive and were accompanied by clinical manifestations of severe sepsis or septic shock. Considering the long interval between both hospitalisations, the patient was enrolled twice. Ultimately, positive cultures were found in 36 patients, generally in 40 samples.

The presence of bacteraemia or infection in relation to positive blood cultures is presented in Table 1.

In the infection group, the infection was likely to have originated from the gastrointestinal tract — 12 cases, including one case from the biliary tract; from the lungs — 4; the pyothorax — 2; while in 11 cases, the aetiology of infection remained unidentified.

In the bacteraemia group, the condition originated from the gastrointestinal tract in 4 cases; from the lungs — 1, while in 6 cases, the aetiology was not detected.

Extended-spectrum β-lactamase (ESβL) strains were found in 3 patients with bacteraemia and in none with the symptoms of infection.

In four *E. coli*-positive patients, the cultures of Proteus mirabilis, Klebsiella oxytoca, Staphylococcus aureus and Streptococcus mitis were also found to be positive. In the bacteraemia group, three patients were also Staphylococcus haemolyticus, Pseudomonas and Enterococcus fecalis positive, respectively.

In the group with ICU-diagnosed infections, 17 patients died, including 12 whose death was probably attributable to E. coli infection. In the bacteraemia group, 8 patients died in the ICU with their deaths unrelated to bacteraemia.

In the case of bacteraemia, positive cultures on day 1 of ICU stay were observed in 4 patients whereas in the remain-

ing 7 cases, bacteraemia was found on days 2, 5, 21, 23, 25, 40 and 42 of the ICU stay.

Likewise, positive cultures with accompanying infection features were noted on day 1 in 11 cases; on day 2 in 6; on day 6 in 2; and on day 7 in another 2. In the remaining 8 cases, positive cultures were demonstrated on days 3, 5, 11, 12, 14, 20, 22 and 31 of the ICU stay.

As the indices currently used to confirm infection or inflammatory reaction, e.g. procalcitonine or CRP, were determined only in individual cases, these data were not analysed. The indices of organ efficiency, not determined in all patients, were also excluded.

DISCUSSION

Under normal conditions, *E. coli* is a commensal and resides in the gastrointestinal tract. However, when unfavourable host conditions are involved, *E. coli*, as well as other Enterobacteriaceae, is likely to become the source of infection, or even lead to death [4].

Moreover, this Gram (–) bacillus is listed amongst the common pathogens causing ventilator-associated pneumonia and catheter-associated urinary infections [5, 6]. In Poland, more patients are mechanically ventilated in comparison to other European countries and the USA, resulting in a higher incidence of ventilator-associated pneumonia (VAP) [7].

According to the literature data, post-renal transplantation infection of the vascular bed with Gram (–) bacteria was an independent factor of transplant failure. The majority of Gram (–) bacteria were *E. coli* [8].

Otherwise, no relationship was found between mortality and *E.coli* genotype in liver recipients [9].

In our material, there were no organ recipients and no cases in which organ donation was considered.

E. coli is one of the leading pathogens inducing nosocomial bacteraemias [10].

In the hospital setting, *E. coli* plays a pivotal role in the aetiology of intra-abdominal infections and hospital-acquired infections. Moreover, its role as a pathogen inducing sepsis, severe sepsis or septic shock is worth stressing [11].

The increasing incidence of isolation of extended spectrum β-lactamase-producing (ESβL) and ciprofloxacin-resistant strains is particularly alarming . In our material, three cases of bacteraemia were associated with ESβL-producing strains. Such strains were not present in any patient with infection. In some East Asian countries, ESβL+ *E. coli* bacteria constitute more than 50% of *E. coli* isolates.

In China, Thailand and India, cases of *E. coli* resistance to ciprofloxacin are common, occurring in 70, 50 and 80% of isolates, respectively [12]. In Poland, this problem is not so relevant, although the observed susceptibility to ciprofloxacin is low, which is most likely associated with the widespread use of fluoroquinolones in ambulatory settings [13].

One of the causes of bacteraemia in severely ill patients may be the translocation of bacteria from the gastrointestinal tract. The pathology is favoured by changes in microbial virulence [14].

Such pathological conditions are common amongst severely ill patients.

The clinical data analysed in our study suggest that translocation from the gastrointestinal tract caused bacteraemia in 4 out of 11 bacteraemia patients and led to infections in 12 cases (41%). However, such estimates are extremely general as they were based on clinical pictures. In a proportion of cases, the clinical picture did not allow one to arrive at any hypothesis. The conclusive results are possible only once the *E. coli* genome is determined from the individual isolates.

Findings in the literature have demonstrated that *E. coli* inducing bacteraemia due to translocation from the gastrointestinal and urinary tract differ in their genotype, which may enable one to assess the risk of infection severity depending on the genome determined [15]. This risk is extremely dangerous in immunocompromised patients [16].

It should however be considered that, with time, the incidence of the isolation of Gram (–) bacteria from the blood, including *E. coli*, has been increasing. The analysis of isolates in patients treated in the University Centre of the Medical University of Gdansk during the period 1997–1999 and 2000–2002 showed an increased incidence of the isolation of Gram (–) bacteria. The most common Gram (–) bacterium isolated between 2000 and 2002 was *E. coli* [17, 18].

Amongst the analysed patients with infection, repeated positive blood cultures were noted in 4 patients during the same ICU stay, namely in the first patient on day 2; in the second on day 4; and in the third on day 6 after the first determinations. In the fourth patient, the first positive culture was an infection whereas the next one (18 days later) was bacteraemia. To decide whether in each case the same strain was involved, the above-mentioned genome testing should be performed.

The differentiation of bacteraemia from sepsis or severe sepsis is essential for its management but even more so for a severity and treatment-associated prognosis. According to Polish studies, the mortality in severe sepsis has reached 55% [19].

Awareness regarding the incidence of Gram (–)-induced sepsis, including *E. coli*, is important as randomised studies have demonstrated that improved outcomes of sepsis treatment, thus reduced mortality, mostly depend on proper antibiotic therapy. It is believed that one's knowledge of the hospital epidemiological condition is relevant in the context of antibiotic therapy.

During the period 2002–2004, the most common Gram(–) bacterium isolated from blood in our hospital was *E. coli*. The Department of Intensive Care has been ranked second amongst wards with the highest number of *E. coli* isolates [13].

E. coli bacteraemias and infections are still relevant in everyday practice as this pathogen, although a commensal, may become pathogenic under favourable conditions. The authors have attempted to assess retrospectively whether the blood culture of *E. coli* was associated with bacteraemia or infection. A substantial limitation of our study, associated with its retrospective character, was the difficulty in obtaining complete clinical data, mainly laboratory results in the period when *E. coli* was cultured. A retrospective analysis of medical records shows that therapeutic management was mainly based on clinical pictures, while laboratory tests were less important. Only a prospective study could provide more data for one to analyse.

E. coli bacteraemias and infections have been and will remain a everyday problem in intensive care units, as well as surgical and internal wards. The differentiation of asymptomatic bacteraemia from infection is essential for rational antibiotic therapy, which is particularly important considering the increasing resistance of microorganisms.

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