Extended-spectrum beta-lactamases (ESBL) in community isolates from North India: frequency and predisposing factors

Extended-spectrum beta-lactamases (ESBL) constitute a growing class of beta-lactamases that are infiltrating our hospitals. They are often plasmid-mediated and are frequently expressed by different *Enterobacteriaceae*. They often remain undetected by current isolation and susceptibility methods.¹

Recently a number of reports have documented the emergence of ESBL in the community in long-term care facilities and ambulatory patients with chronic conditions. These reservoirs may feed back into the pool of ESBL in the hospital environment.² Our retrospective analysis was carried out to describe the prevalence of ESBL-producing organisms amongst our isolates and the proportion that were from community or non-hospitalized patients. We also describe the prevalence of factors that predispose to ESBL production in these patients.

The study was conducted in the Department of Microbiology, Government Medical College and Hospital, Chandigarh, between January and October, 2004. Three hundred unique *Enterobacteriaceae* isolated from clinical samples were tested for ESBL production. Antimicrobial susceptibility testing was performed by the disk diffusion method according to NCCLS guidelines.³ ESBL screening was by disk diffusion⁴ and confirmation by the double disk synergy test (DDST).⁵

We reviewed the medical records of patients with community onset infection with ESBL producers, for demography, co-morbidity, and history of previous antimicrobial therapy and prior hospitalization. Community onset infections were defined as individuals who did not have a history of hospitalization in the preceding three months and who were either outpatients or admitted patients who had had their first positive culture results from samples obtained within 48 h of hospital admission. Other hospitalized patients and those hospitalized within three months were deemed to have nosocomial infections.⁶

Out of the 300 bacterial strains, 72 (24%) were ESBL producers. Fifty of these 72 were from patients who met the criteria of community onset infection. Among these, 44 were *Escherichia coli* and six were *Klebsiella pneumoniae*. The total numbers of *E. coli* and *K. pneumoniae* isolated during the study period from the community-associated infection cases were 184 and 30, respectively. Clinical samples from which these ESBL strains were isolated included urine (36), pus (10), and sputum (4). On reviewing the medical records of the 50 patients with ESBL strains from community onset infection the following percentages of predisposing factors were found: 50% (25) of the patients were >60 years of age, 74% (37) were male patients, 76% (38) had a history of previous use of second or third generation cephalosporins, 74% (37) had a history of previous use of quinolones, and 48% (24) had a history of hospitalization prior to the immediate past three months. Only 24% (12) of the patients had a history of diabetes mellitus (DM) and only 12% (6) of the patients had *K. pneumoniae* infection.

A study carried out by Mathur et al. reported the rate of ESBL producers to be 68% and another by Tankhiwale et al. found it to be 48%.⁷ This variation may be real and be due to different antibiotic programs or it could reflect differences in study design.

A high rate of resistance to various antibiotics was seen in our study (amikacin 24%, gentamicin 75%, ciprofloxacin 65%, ceftazidime 88%, cefotaxime 90%, ceftiraxone 87%, cephrine 62%, amoxicillin/clavulanic acid 69%) although all the ESBL producers were susceptible to imipenem and piperacillin/tazobactam. Other workers have also reported high rates of antimicrobial resistance among ESBL producers.⁷ These high rates could be because of poorly directed therapy and over-the-counter sales.

Factors predisposing to ESBL production, as reported by Colodner et al.,⁹ were common in our study: age over sixty years, male sex, prior history of taking antibiotics, and hospitalization. In addition to these factors, Rodriguez Bano et al. reported DM and recurrent urinary tract infection (UTI) as risk factors for ESBL production.⁶ In our study 12 of 50 community patients with ESBL producers had associated DM. Pitout et al. studied ESBL in *E. coli* from community onset infections and found females to be commonly infected.¹⁰ In our study most ESBL-producing *E. coli* were from males. This could be explained on the basis that elderly male patients are prone to drug resistant strains because of prior antibiotic therapy and hospitalization. However, study design differences are just as likely. Ours is not a study of community-acquired UTI, where most infections are treated empirically, but is based on samples sent to the hospital laboratory. The population studied may therefore be biased by medical and social factors that affect a sample being submitted. Our study does, however, show the high prevalence of ESBL in ambulatory patients who had not been admitted in the near past. We found DDST to be an easy, cheap, sensitive and easily reproducible test.

Our results show that the non-hospitalized community that submits samples for analysis, from which many are hospital outpatients, has become infiltrated with ESBL enzymes. Although this is a self-selecting group, heightened vigilance and further studies regarding dissemination of ESBL in the community should be undertaken.

Conflict of interest: No conflict of interest to declare.

References

Hemophagocytosis and pulmonary involvement in brucellosis

We report the case of a 45-year-old woman who presented with fever, hepatosplenomegaly, jaundice, rash, and tachypnea. Wright’s serum agglutination and 2-mercaptoethanol (2-ME) tests were both positive in the range of 1/2560 and hemophagocytosis was shown in bone marrow aspiration.

The illness began with flu-like symptoms 15 days earlier. Four days before admission she had developed jaundice, headache, myalgia, malaise, anorexia, nausea, and a productive cough. There was no history of previous disease. Her occupation involved all aspects of animal husbandry including the slaughter and skinning of animals. On physical examination, icteric sclera, blood clots in the pharyngeal pouch, ecchymosis (Figure 1), and tenderness in the right upper quadrant were found. Her platelet count at the time of admission was $13 \times 10^9$ cells/L. Twenty-four hours after admission she developed epistaxis. Oral ribavirin was started with a probable diagnosis of Crimean-Congo hemorrhagic fever.

On the second hospital day, laboratory findings were as follows: hemoglobin (Hb) 11.2 g/dL, LDH 2345 IU/L, alkaline phosphatase 391 IU/L, SGOT 277 IU/L (N < 39), and SGPT 322 IU/L (N < 40). Her white blood cell (WBC) count was $5.6 \times 10^9$ cells/L, erythrocyte sedimentation rate was 8 mm/h, direct bilirubin 15.4 mg/dL, total bilirubin 22.1 mg/dL, Wright’s agglutination test 1/2560, and 2-ME was 1/2560. Owing to positive Wright’s agglutination and 2-ME tests, ribavirin was changed to doxycycline plus gentamicin.

Four days after admission laboratory tests revealed pancytopenia: platelet count $12 \times 10^9$ cells/L, Hb 8.5 g/dL, and WBC $3.5 \times 10^9$ cells/L. Bone marrow aspiration revealed an increase in histiocytic lineage and phagocytosis of nucleated red blood cells and platelets (hemophagocytosis). The cultures of bone marrow were negative. Other laboratory tests revealed normal blood cultures and serum ferritin > 1000 ng/mL.

Five days after admission, high resolution computed tomography of the chest was performed due to persistent tachypnea and rales, and showed consolidation in both lungs. After three days of treatment with hydrocortisone (200 mg/day) and anti-brucellar drugs, the platelet count increased, liver enzymes decreased (SGPT 130 IU/L, SGOT 91 IU/L), and prothrombin time (PT) and partial thromboplastin time (PTT) returned to normal.

Mild hematologic abnormalities are common in brucellosis and usually subside with treatment of the disease itself. Thrombocytopenia may be severe and associated with purpura and bleeding. Steroids have been recommended in severe thrombocytopenia associated with human brucellosis. Severe disorders such as hemophagocytic syndromes have also been described. Hemophagocytic syndrome is associated with a broad spectrum of diseases such as viral, bacterial and mycobacterial diseases. Signs and symptoms of hemophagocytic syndromes are often similar to common infections or mimic fever of unknown origin or hepatitis. Fever, splenomegaly, and hepatomegaly are the most common clinical findings and lymphadenopathy, jaundice, and rashes can also be found. Hemophagocytic syndrome may result in pulmonary involvement.

In daily practice, the diagnosis of brucellosis is established by a positive Wright’s agglutination test in a titer of $>1/160$ in association with an appropriate clinical setting. The brucella infection in our patient was established with strongly positive serology (standard tube agglutination (STA) test).

![Figure 1](image-url) Ecchymosis of the lower limbs in a patient with brucella-induced hemophagocytosis.