Excess mortality due to KPC-producing Klebsiella pneumoniae in liver transplant recipients

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Outcome of carbapenem resistant *Klebsiella pneumoniae* infection in tertiary care centre in India

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Background: CRE rates in India are between 15% to 60% in various studies. Poor infection control practices have ensured that the incidence of these organisms is on the rise. We hope to highlight the impact of these infections in terms of mortality and length of stay in hospital.

Methods & Materials: Consecutive patients admitted during 24 months (1st January 2011 to 31st December 2012) with CR - Klebsiella isolates from any site where included. The patient was evaluated clinically and with APACHE-II scores done at a time nearest to the sampling and also followed up for modification of antibiotic therapy based on culture reports, and finally the outcome (death or discharge as cured from the hospital). Assuming a mortality of 40% for serious CR-Klebsiella infections (BSI) from published data, sample strength of 58 was calculated for adequately powering the study at 95% CI & 5% error. Fischer's Exact Test was used for analysing the statistical significance of outcome differences between Colistin based therapy and non-Colistin based therapy. Absolute mortality and Severity Adjusted Mortality (SAM = observed mortality/expected mortality as per APACHE-II scores X 100) were calculated.

Results: A) Out of 87 isolates 59 were proven infections. Most common site of infection was urinary, followed by blood stream infection, pneumonia and skin & soft tissue.

B) The mean age of cases was 53.6 years. 64% were males and 36% were females

C) The absolute mortality in infections was–25% for UTI, 46% for Pneumonia, 33.3% for BSI and 9.1% for SSTI. The Severity Adjusted Mortality was 100 for UTI, 60.6 for SSTI, 184.4 for pneumonia and 222.2 for BSI.

D) The ALOS was 20.2 days, 42% had more than 7 days of hospitalization before isolating the CR- Klebsiella.

Conclusion: Carbapenem resistant Klebsiella infections are associated with high mortality (SAM > 100 especially for pneumonia and blood stream infections). The study was possible not powered to make a comparison between various antibiotic regimens. CR Klebsiella infections are associated with significantly prolonged length of stay–both before isolation and after infection.

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Excess mortality due to KPC-producing *Klebsiella pneumoniae* in liver transplant recipients

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Background: Nosocomial infections in immunocompromised patients frequently originate from the Gram-negative bacterium *Klebsiella pneumoniae* (KP). Treatment options are considerably restricted by the emergence of carbapenem-resistant strains. Organ transplant recipients are especially at risk for peri-interventional infections by multidrug-resistant bacteria, however, only little is known on the impact of *K. pneumoniae* carbapenemases (KPCs) producing pathogens in this setting yet.

Methods & Materials: Among 103 patients either colonized or infected with KPC-2-producing KP (KPC-2-KP) during a large hospital outbreak, we identified 9 KPC-positive patients, who had undergone orthotopic liver transplantation (LTx) between 15.09.2010 and 14.09.2011 at the Leipzig University Hospital, Germany. Presence of KPC-2-KP was confirmed by culture and molecular typing was performed using pulsed-field gel-electrophoresis (PFGE). The data from these n = 9 LTR were retrospectively compared to a matched cohort of n = 35 LTR (transplanted from 2008 to 2011) with proof of invasive infections due to carbapenem-susceptible *Klebsiella* spp. strains (69% KP, 31% *K. oxytoca*), including a high proportion of ESBL-producers (71%). All patients were followed up for 6 months after LTx.

Results: 89% (8/9) of KPC-2-KP-positive LTR progressed to infection (50% pneumonia, 25% surgical site infections, 25% tertiary peritonitis), and in 56% (5/9) bloodstream infection with KPC-2-KP was confirmed. Matched comparison showed a hospital mortality rate of 78% (LTR with KPC-2-KP) compared to 34% in the remaining patients ($P = 0.027$). Six-month survival in KPC-positive LTR (22%) was significantly lower compared to LTR with sensitive *Klebsiella* strains (70%), and LTR with ESBL-producing *Klebsiella* strains (64%) ($P < 0.05$).

Conclusion: We conclude that colonization with carbapenem-resistant *Enterobacteriaceae (*CRE) like KPC-2-KP in LTR leads to high infection rates and excess mortality. Therefore, frequent screening for CRE in patients on LTx waiting lists appears reasonable. Although active surveillance studies have demonstrated high infection rates associated with excess mortality, colonization with CRE is so far not considered a contraindication to LTx. This position might need re-evaluation with respect to the fundamental difficulties of graft allocation due to severe organ shortage in countries like Germany. In our opinion, currently available data do not justify to consider patients with end-stage liver disease and evidence of persistent colonization by CRE failing decolonization efforts for LTx.

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