REFERENCE

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P250 INCIDENCE, CLINICAL PROFILE AND OUTCOMES OF VENTILATOR-ASSOCIATED PNEUMONIA IN A TERTIARY HOSPITAL

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Background Pneumonia is still the most important nosocomial infection among critically ill patients receiving mechanical ventilation despite advancement in the diagnostic technology available, introduction of new antimicrobials and employment of preventive strategies. Our aim was to prospectively identify the occurrence of ventilator-associated pneumonia (VAP) in a tertiary hospital as well as to determine its clinical profile and outcomes.

Methods A prospective, observational study was performed including 52 patients with VAP in a tertiary hospital. All adult patients admitted who required mechanical ventilation regardless of site of care was included and followed up until successful weaning, discharge or death.

Results During the 12-month study period (1 May 2009–30 April 2010), a total of 52 patients (7.6%) developed VAP among the 686 patients who received mechanical ventilation. Most common co-morbid conditions documented were diabetes mellitus and hypertension. Higher APACHE II scores ($p \leq 0.001$), inappropriate antimicrobial use ($p=0.027$) and the presence of underlying malignancy ($p=0.03$) are correlated with mortality. The most common pathogen isolated was *Pseudomonas aeruginosa* (23%) and carbapenems as the most commonly used antimicrobial. Mortality rate was 38.5%. Non-survivors had numerically longer ICU stay and length of mechanical ventilation (Abstract P250 Table 1).

Abstract P250 Table 1

	Non-Survivors (n=20)	Survivors (n=32)	Total (n=52)	p-value
Age	68.5 ± 14.68	63.59 ± 17.26	65.48 ± 16.34	0.297 (NS)
Gender				
Male	9 (45%)	21 (65.63%)	30 (57.69%)	0.162 (NS)
Female	11 (55%)	11 (34.38%)	22 (42.31%)	
Ward Type				
Clinical division	5 (25%)	11 (34.38%)	16 (30.77%)	0.549 (NS)
Pay division	15 (75%)	21 (65.63%)	36 (69.23%)	
Co-morbidities				
Hypertension	6 (30%)	16 (50%)	22 (42%)	0.25 (NS)
Diabetes Mellitus	11 (55%)	14 (44%)	25 (48%)	0.57 (NS)
COPD*	2 (10%)	2 (6%)	4 (8%)	0.63 (NS)
Underlying Malignancy	7 (35%)	3 (9%)	10 (19%)	**0.03**
Renal Failure	1 (5%)	6 (19%)	7 (13%)	0.23 (NS)
CAD**	4 (20%)	2 (6%)	6 (12%)	0.19 (NS)
Reason for Intubation				
Medical	17 (85%)	21 (65.63%)	38 (73.08%)	0.200 (NS)
Surgical	3 (15%)	11 (34.38%)	14 (26.92%)	
VAP Onset				
Early	11 (55%)	22 (68.75%)	33 (63.46%)	0.382 (NS)
Late	9 (45%)	10 (31.25%)	19 (36.54%)	
Definite Etiology				
Without	5 (25%)	9 (28.13%)	14 (26.92%)	1.000 (NS)
With	15 (75%)	23 (71.88%)	38 (73.08%)	
With Monomicrobial	*9 (60%)*	*13 (56.52%)*	*22 (57.89%)*	
With Polymicrobial	*6 (40%)*	*10 (43.48%)*	*16 (42.11%)*	
Appropriateness of Empiric Antibiotics				
Yes	4 (20%)	18 (56.25%)	22 (42.31%)	**0.027**
No	9 (45%)	6 (18.75%)	15 (28.85%)	
Unknown	7 (35%)	8 (25%)	15 (28.85%)	
Number of Drugs				
Monotherapy	10 (50%)	18 (56.25%)	28 (53.85%)	0.777 (NS)
Combination	10 (50%)	14 (43.75%)	24 (46.15%)	
Concomitant Infection				
With	9 (45%)	20 (62.5%)	29 (55.77%)	0.260 (NS)
Without	11 (55%)	12 (37.5%)	23 (44.23%)	
Mean APACHE II score	27.25 ± 6.26	20.88 ± 5.59	23.33 ± 6.59	**0.000**

*Tested combining High and Very High levels;
Continuous Variables are compared using Independent T-test
Categorical Variables are compared using Chi-Square Test/Fisher's Exact Test
*Chronic Obstructive Pulmonary Disease
**Coronary Artery Disease

Conclusion In our setting, current VAP incidence rate is 7.6% with mortality of 38.5%. This highlights the current magnitude of VAP which should prompt hospital administrators and health care workers to complement rational antibiotic use with non-pharmacologic strategies to at least decrease VAP incidence and alleviate its burden especially in a developing country.

P251 FLOW CYTOMETRIC DETECTION OF INTRACELLULAR ACTIVATION MARKERS OF PULMONARY CELLS DURING ACUTE LUNG INJURY

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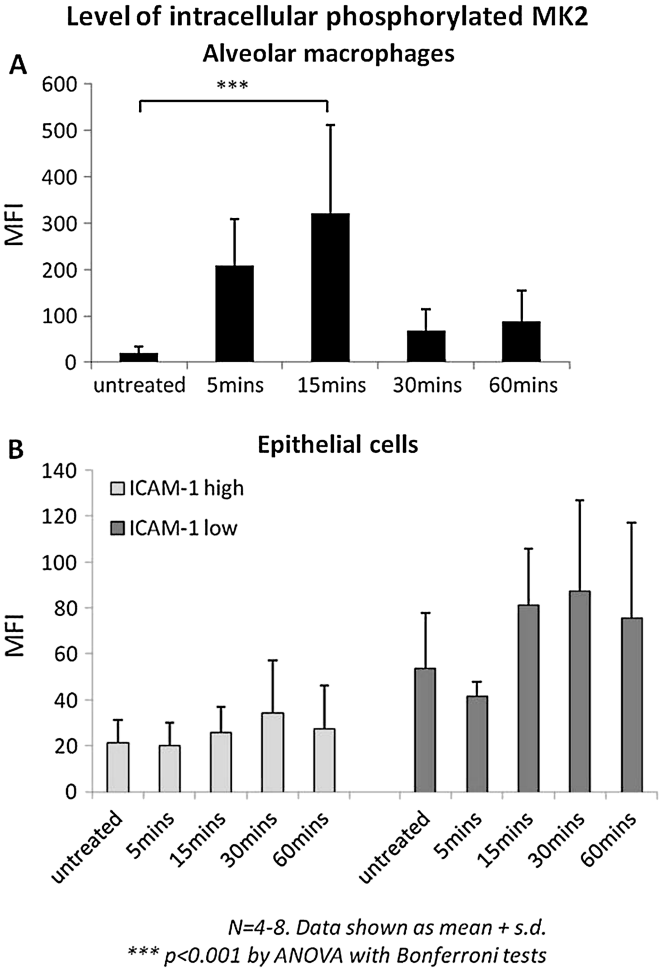
Background Activation of intracellular signalling cascades such as mitogen-activated protein (MAP) kinase pathways has been implicated in various animal models of acute lung injury. However, such data rely almost exclusively on measurements within whole lung homogenate samples, so little information is available regarding cell type specific processes. In order to address this, we have developed a flow cytometric technique to identify discrete pulmonary cell populations and examine their early activation in terms of phosphorylation of intracellular MAPkinase pathway intermediates (ERK, p38 and its downstream target MK2).



Abstract P251 Figure 1 Level of intracellular phosphorylated MK2. A. Alveolar macrophages. B. Epithelial cells.

Methods Anaesthetised C57BL6 mice were given an intratracheal 20 µg dose of lipopolysaccharide (LPS). Mice were sacrificed at various time points, their lungs were removed, immersed in a buffer to fix and permeabilise cells, and a single cell suspension was produced by mechanical disruption. After incubation at 37°C the cell suspension was washed and centrifuged. Samples were stained at room temperature in the dark with antibodies to identify alveolar macrophages (AM) and epithelial cells (AEC), and to measure the intracellular levels of active phosphorylated forms of ERK, p38 and MK2. Finally the cells were washed and resuspended for flow cytometric analysis.

Results AM showed a rapid increase in levels of phosphorylated MK2 (see Abstract P251 Figure 1) as well as p38 and ERK on stimulation by intraalveolar LPS. As MK2 showed the most robust response, we determined its phosphorylation in AEC. Those AEC expressing low levels of surface ICAM-1 (likely type II pneumocytes) showed a pattern of increased MK-2 phosphorylation, while ICAM-1 high expressing AEC (type I pneumocytes) did not show a clear response to LPS stimulation.

Conclusion We have developed a method of investigating activation of individual cells within the lung using flow cytometry, in terms of intracellular MAPkinase phosphorylation. Our data show that AM are rapidly activated upon stimulation by intraalveolar LPS, whereas AEC show signs of delayed activation with type II pneumocytes more responsive than type I cells. Applying this technique to other models, in which alternative cell types and/or pathways may be involved, will enhance our understanding of cellular activation and interactions during acute lung injury.

P252 A PHYSIOLOGICAL CHARACTERISATION OF INJURY, INFLAMMATION AND RESOLUTION IN MURINE ASPIRATION PNEUMONITIS

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Introduction and Objectives Aspiration pneumonitis is an important risk factor for acute lung injury/acute respiratory distress syndrome (ALI/ARDS).[1] Animals models of ALI should ideally mimic the human situation, although to date none fully reflect the complex pathophysiology involved. Our objective was to develop, optimise and characterise a model of acid aspiration that would closely resemble clinical ALI/ARDS including both inflammatory and recovery phases. While longer-term animal models of acid aspiration have been utilised, their clinical applicability has been limited by high mortality or use of unilateral pulmonary instillation[2].

Methods C57Bl6 mice were anaesthetized, orotracheally catheterised and instilled with 75 µl of 0.1 M hydrochloric acid. They were recovered with FiO_2 of 0.4 for 6 h and then placed in room air. At pre-determined time points they underwent tracheostomy, low tidal volume ventilation (8 ml/kg), and arterial catheter placement. Respiratory system mechanics and arterial oxygenation were determined, and following termination, bronchoalveolar lavage (BAL) was sampled for neutrophil infiltration and total protein concentration.

Results Following acid aspiration mice showed significant weight loss, decreased PaO_2:FiO_2 ratios and increased respiratory system elastance compared to untreated controls. There was significant pulmonary endothelial/epithelial leak as measured by BAL protein concentration, as well as substantial neutrophil influx. Changes in all of these parameters were transient, peaking on days 1–3 and then resolving to near baseline by day 10 (Abstract P252 Table 1).

Abstract P252 Table 1

	Control	Day 1	Day 2	Day 3	Day 5	Day 10
Weight Loss (%) (N=5-11)	–	−7.0± 2.3	−13.3± 4.9	−13.3± 4.0	−7.3± 2.5	−2.9± 1.9
PaO_2:FiO_2 (N=3–5)	507± 37	162± 97***	310± 74*	158± 69**	359± 97	538± 11
Respiratory Elastance ($cmH_2O/\mu l$) (N=3–4)	0.028± 0.002	0.061± 0.018***	0.065± 0.008***	0.035± 0.003	0.032± 0.002	0.027± 0.001
BAL Protein Conc. (mg/ml) (N=3–6)	0.15± 0.02	4.86± 0.47***	3.36± 0.56***	1.72± 0.89**	0.73± 0.20	0.31± 0.09
BAL Neutrophil Count ($\times 10^4$/ml) (N=3–4)	0.002± 0.004	5.7± 3.8	28.4± 5.1***	6.60± 0.63	0.47± 0.19	0.003± 0.001

All timepoints compared with One-Way Analysis of Variance with Bonferroni test. ***p<0.001, **p<0.01, *p<0.05 vs control.

Conclusion In this study, we describe a translational model of acid-induced lung injury that shows significant injury and inflammation resolving over a 10-day period. It shows many characteristics of clinical ALI/ARDS including severe hypoxaemia, worsening respiratory mechanics, alveolar-capillary barrier permeability, and neutrophilic infiltration within the alveolar space. This resolving model of aspiration pneumonitis may allow further elucidation of the pathophysiological mechanisms of ALI/ARDS and its resolution, in particular oedema formation and inflammatory cell recruitment.

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P253 PULMONARY INFILTRATES IN HIV NEGATIVE IMMUNOCOMPROMISED PATIENTS: OUTCOME AND PREDICTIVE FACTORS

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Introduction The incidence of pulmonary complications in immunocompromised patients is on the rise mainly driven by increased organ and bone marrow transplants, more aggressive chemotherapy and novel immunosuppressants.[1] Mortality rates in HIV negative immunosuppressed patients vary between 40–85%.[1–3] Prognostic factors have been previously described in these patients and these include need for mechanical ventilation and delay in diagnosis.[2]

Aims To describe the characteristics of immunocompromised HIV negative patients presenting with pulmonary infiltrates and to examine the factors that lead to increased mortality.

Methods All HIV negative immunocompromised patients who had bronchoalveolar (BAL) samples taken from January 2007 to January 2010 were identified from laboratory data. Their baseline demographics, immune status, clinical presentation, radiological picture and blood results at the time of BAL sampling were obtained from hospital records. The influence of various categorical variables on mortality was evaluated using Chi-square test. Logistic regression was then used to quantify the impact of each of these variables and obtain OR.

Results 87 patients (33 women) with a median (range) age of 62 (21–87) years were studied. Overall mortality was 49% (42