What are the Risk Factors Associated with *Pneumocystis jirovecii* Pneumonia (PCP) Amongst Renal Transplant Recipients?

**Introduction**

Renal transplant recipients (RTRs) are at great risk of infection largely due to the immunosuppressive therapy used to prevent organ rejection. The greatest risk of acquiring infection is within the first 6 months and studies have shown that around 50% of RTRs will have had an infection in the first year following transplant (National Kidney Foundation, 2012). This study focuses particularly on the acquisition of *Pneumocystis jirovecii* pneumonia (PCP) amongst RTRs. PCP is an opportunistic fungal pathogen which can cause life threatening pneumonia and most commonly occurs 6–8 weeks after transplant (KDOQI, 2009). Clusters of cases amongst the renal population are increasing (de Boer et al, 2011) and it has a mortality rate of up to 49% (Le Gal et al, 2012). PCP has been described as a re-emerging public health problem (Chapman et al, 2013) and large outbreaks have been recorded throughout the UK. This study focuses on a renal transplant unit over a period of 1 year in which 18 cases of PCP were identified.

**Aim of the Study**

The main aim of this study was to identify individual risk factors which contributed to the development of PCP during the outbreak amongst this group of renal transplant recipients and whether these risk factors had been identified in any other outbreaks. The recommended prophylaxis was also reviewed to ascertain whether it was sufficient to prevent similar outbreaks. Lastly, it was hoped that any infection prevention and control or therapeutic interventions which are effective in preventing acquisition of PCP would be identified. If this were to be the case it was hoped that practice could be changed for the better.

**Methodology**

Following notification of 3 cases of PCP on the renal transplant unit, investigations began by the local Infection Prevention and Control Team (IPCT). The lab database was used to identify any cases in the previous year of which there were 4. No known source or cause of the outbreak was identified. The cluster of cases which followed brought the total number of cases involved into the outbreak to 18. Prior to the outbreak the incidence of PCP within the unit was low (1-2 cases per year).

This raised questions around risk factors amongst this patient group which may have been associated with the acquisition of PCP leading to commencement of the study. A matched case control study was chosen for this study to eliminate confounding variables. It was conducted in a 22 bedded renal transplant unit.

Definitions for inclusion in the study were formulated using the following criteria;

- Positive isolate of *Pneumocystis jirovecii* in throat swabs, sputum samples or bronchoalveolar lavage.
- Clinical Symptoms in keeping with PCP.
- Interstitial shadowing on chest x-rays.

In applying these definitions, 4 cases were excluded from the study leaving a total of 14. Each of the 14 cases were matched with a control case according to recipient age at time of transplant and day of diagnosis of the disease within a 2 year range. All 28 cases were fully reviewed and the same data set collected for each. A literature search provided a list of possible risk factors on which to base the data collection including age, sex, race, type of transplant and any rejection episodes, age at time of transplant, immunisation and PCP prophylaxis regimes, Cytomegalovirus (CMV) status, lymphocyte count before transplant and PCP prophylaxis. For PCP cases, the time between transplant and development of PCP was also collected alongside the age at time of PCP diagnosis. Data was collected using Microsoft excel and then each category and sub category was reviewed which included environmental audit results, audits of practice within the ward and environmental issues, previous and existing. The data was then reviewed for any statistical significance between risk factors and development of PCP and any possible links to practice or the environment.

**Results & Discussion**

- **Organ Rejection Episodes**
  
  Statistically cases who experienced 1 or more episode of rejection were more likely to develop PCP than those who had no rejection episodes. Rejection episodes are often treated with increased immunosuppressants further exposing the patient to greater risk and subsequently PCP. The administration, timing and duration of prophylaxis remains varied between RTRs. In prescribing prophylaxis clinicians must consider cost, efficacy and potential side effects associated with prophylaxis. Some RTRs have little or no identified cases of PCP identified and would argue that PCP prophylaxis is unnecessary. This study would suggest that prophylaxis should be administered for 6 months post transplant and after during every rejection episode at the very least to create a herd immunity amongst the vulnerable renal transplant population.

- **Typing results**
  
  Typing revealed only 3 cases shared the same strain of PCP. Whilst this may suggest possible acquisition of PCP in the community, typing maps highlighted cross over between type matched cases within the clinic setting which could suggest possible cross transmission. 1 case was admitted as an inpatient to the renal unit from clinic with suspected PCP. The timeline showed that 2 other cases attended clinic on the same day and subsequently tested positive for PCP.

- **Outbreak Investigations**
  
  Environmental audits of the inpatient wards scored well in general although blood stained items of equipment were identified. It was also noted that the area was very cluttered and there was little storage for large volumes of equipment. Depending on dialysis, requirements for side rooms and demand for high acuity care, patients also moved between the 3 areas frequently as did staff using the centre ward as a main route between areas. Alongside typing and timeline findings, this study would suggests that such conditions increase the risk of environmental contamination and possible cross transmission of PCP.

- **Future study**

  Future studies looking at exposure within clinics during periods of immunosuppression and rejection may yield a greater understanding as to the acquisition of the disease.

**Conclusion**

This study has highlighted the complexities in managing an outbreak of PCP, the unknown risk factors associated with it's acquisition and the lack of understanding regarding its epidemiology. The main finding of this study was a statistically significant association between rejection episodes and PCP. Recommendations from the study incl: Application of Transmission Based Precautions (TBPs) for all suspected/confirmed PCP patients, PCP prophylaxis for 6 months after transplant and 6 months after rejection episode, inclusion of PCP in alert organism list. The findings of this study have resulted in a review of post transplant PCP prophylaxis and prophylaxis following a rejection episode within the local renal transplant unit. Changes to both have now been implemented.

**References**


**Acknowledgements**

Thanks to Dr Teresa Inkster (Consultant Microbiologist, GGC), Simon Packer (Healthcare Scientist, HPS), Dr Rory Gunson (Consultant virologist).