

# **An Assessment of Empiric Management Practices of Common Infections in Solid Organ Transplant Recipients — A Retrospective Cohort Study**

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## **Background:**

Infections are a major cause of morbidity and mortality in solid organ transplant (SOT) recipients. All SOT recipients have been noted to be at a higher risk for infection, although the specific type and location differ depending on the type of SOT performed - lung transplant recipients are at the highest risk for pneumonia, kidney transplant recipients for urinary tract infections, liver transplant recipients are commonly affected by post-transplant cholangitis, and all SOT recipients in general have an increased susceptibility to bacteraemia. The development of these infectious diseases can adversely affect patient outcomes, leading to increased rates of mortality and graft dysfunction<sup>1-3</sup>.

Antimicrobial therapy is often initially empiric, relying mostly on clinical presentation and thus employing broad-spectrum agents in an effort to treat multiple suspected pathogens. Once microbiological data is available however, guidelines generally suggest that the treatment should be de-escalated, and that the spectrum should be narrowed.

Based on local susceptibility patterns, standardized antimicrobial treatment guidelines for infectious syndromes may contribute to improved clinical care. Previous studies examining rates of guideline-concordant therapy have found adherence to be low. Further, controversy exists as to whether complying with guidelines is actually associated with improved patient outcomes<sup>6-11</sup>.

Some studies have shown that adherence to guidelines does not have a significant impact on patient outcomes<sup>8, 12-15</sup>. Conversely, other papers explicitly oppose these findings by concluding that guideline compliance is associated with improved patient outcomes<sup>4-6, 10, 11, 16-25</sup>. Despite

these differing conclusions however, most of the papers dissenting on adherence to specific guidelines agree that a narrower spectrum of antimicrobial therapy should be utilized<sup>8, 9, 21</sup>.

The variety of conclusions drawn from these papers suggests that further studies must be conducted in order to investigate the clinical significance of guideline adherence when it comes to patient management. Additionally, although several studies examining the efficacy of guidelines exist, there is a distinct lack of research on efficacy for SOT populations in particular. Our study thus seeks to assess the rate of therapeutic compliance with local standard guidelines in the treatment of common infections in solid organ transplant recipients, and their associated outcomes.

#### **Methods:**

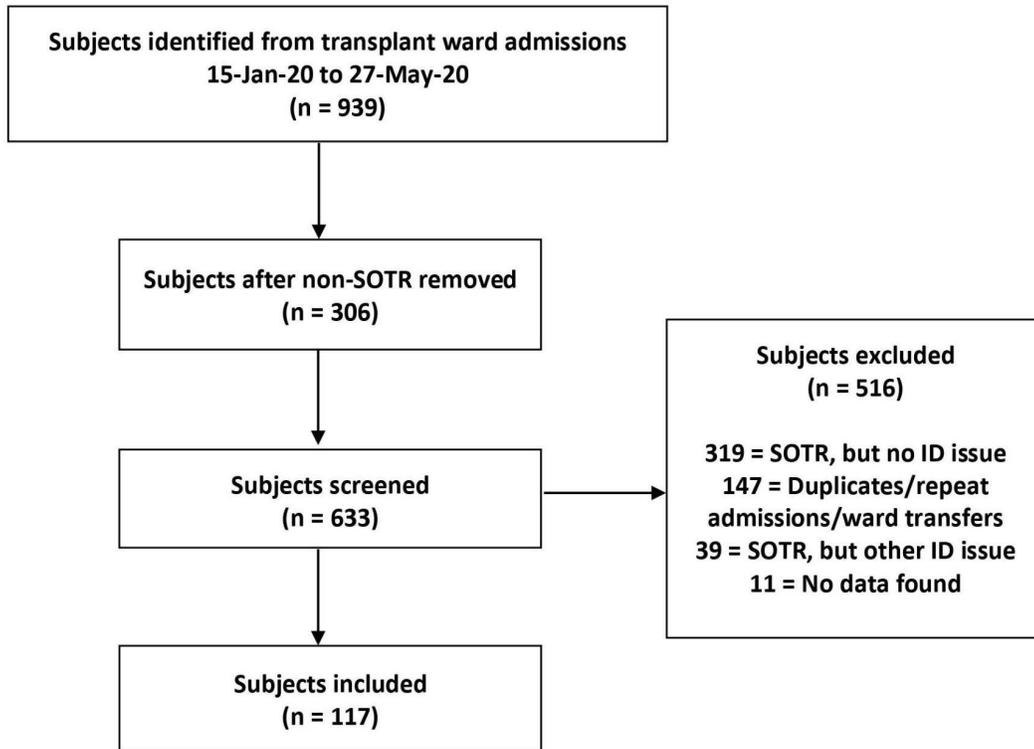
In this single-centre retrospective cohort study, we reviewed consecutive adult solid organ transplant recipients admitted to the transplant floor from January 2020 till May 2020 for the treatment of an infectious syndrome of interest for study inclusion.

Subjects who were not SOT recipients, transplant recipients who did not develop an infectious syndrome or developed an infectious syndrome of non-interest, and subjects who were repeat admissions or ward transfers were excluded. Patients were followed until discharge or for 30 days following the date of diagnosis, whichever came first. Data was extracted from electronic medical records, then collated into tables.

Clinical outcomes were analyzed using Fisher's Exact Test or Mann-Whitney tests for categorical and continuous variables, respectively. Outcomes of interest include length of stay, ICU stay, readmission within 30 days, C. difficile infection within 30 days, rejection within 30 days, graft loss within 30 days, and death within 30 days.

**Results:**

Between January 15, 2020 and May 27, 2020, 939 subjects were identified for study inclusion (Fig. 1). Of these, 306 were excluded as they were not solid organ transplant recipients. 633 subjects remained after non-SOT recipients were excluded. 516 of the 633 were excluded: 319 were SOT recipients but were not treated for any infectious syndrome, 147 were duplicates, repeat admissions, and ward transfers, and for 11 subjects no data could be obtained. Of the 475 SOT recipients admitted to the transplant floor, 156 (33%) were admitted with infectious syndromes. Ultimately, guidelines were applicable to 117 patients, comprising the following 122 syndromes: 51 pneumonia, 34 urinary tract infections, 22 bacteremia, and 15 intra-abdominal syndromes (Table 1).



**Figure 1: Study Flow Diagram**

56% of patients included in the study were male, and the mean age was 57 years. The median Charlson Comorbidity Index score across all syndromes was 3. 67% of patients with an intra-abdominal infection were liver transplant recipients, 56% of patients with a urinary tract infection were kidney transplant recipients, and 49% of patients with pneumonia were lung transplant recipients. Intra-abdominal infections were found to occur the earliest, at a median time of 9 months post-transplant.

**Table 1: Baseline Characteristics of Patient Cohort**

Characteristic	Infectious Syndrome				
	Pneumonia (n=51)	UTI (n=34)	Bacteremia (n=22)	Intra-abdominal (n=15)	All syndromes (n=122)
Age, y, mean $\pm$ SD	60 $\pm$ 11.83	56 $\pm$ 16.62	57 $\pm$ 9.01	52 $\pm$ 14.70	57 $\pm$ 13.38
Male sex (%)	37 (73%)	10 (29%)	13 (59%)	8 (53%)	68 (56%)
Charlson Comorbidity Index, median	3	3	2	3	3
Organ n, (%)					
Kidney	12 (24%)	19 (56%)	5 (23%)	0 (0%)	36 (30%)
Liver	9 (18%)	6 (18%)	9 (41%)	10 (67%)	34 (28%)
Lung	25 (49%)	8 (24%)	3 (14%)	1 (7%)	37 (30%)
Heart	2 (4%)	0 (0%)	2 (9%)	1 (7%)	5 (4%)
Kidney-Pancreas	2 (4%)	1 (3%)	1 (5%)	2 (13%)	6 (5%)
Other	1 (2%)	0 (0%)	2 (9%)	1 (7%)	4 (3%)
Time since transplant, months, median	38	54	10	9	28

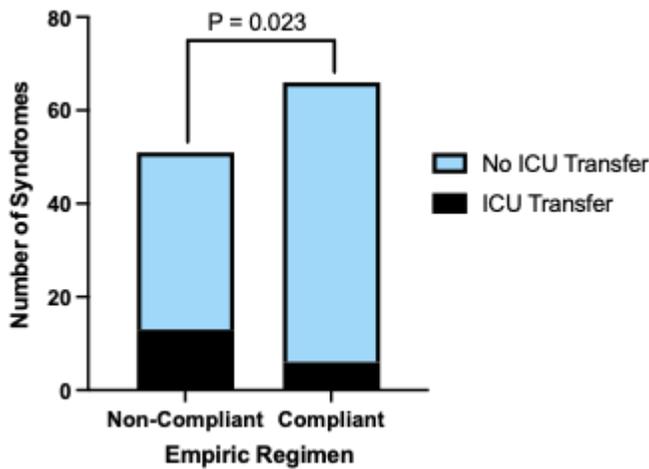
47% (n=66) of patients were empirically treated with guideline-compliant therapy, while 66% (n=81) of patients were provided guideline-compliant tailored therapy (Table 2).

**Table 2: Outcomes of compliant vs. non-compliant treatment in patients receiving antimicrobial therapy for an infectious syndrome**

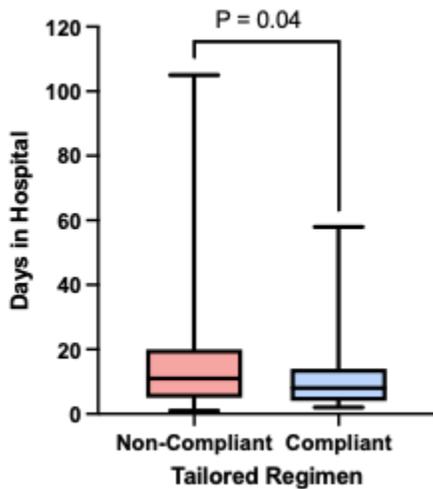
	Empiric Therapy			Tailored Therapy		
	Compliant	Non-Compliant	P value	Compliant	Non-Compliant	P value
<b>All Syndromes (n=122)</b>	n=66	n=51		n=81	n=41	
ICU Stay	9%	25%	<b>0.023</b>	11%	24%	n.s.
Length of stay, median, days	8	9	n.s.	8	11	<b>0.038</b>
Readmission within 30 days	29%	33%	n.s.	32%	32%	n.s.
C. diff infection within 30 days	0%	2%	n.s.	0%	2%	n.s.
Rejection within 30 days	3%	2%	n.s.	1%	5%	n.s.
Graft loss within 30 days	5%	2%	n.s.	4%	2%	n.s.
Death within 30 days	8%	2%	n.s.	4%	7%	n.s.

Non-compliance with empiric management guidelines was found to result in a significantly higher proportion of patients requiring ICU transfer when compared to compliance (P=0.2) (Fig.

2). Non-compliance with tailoring protocols resulted in an increased overall length of stay ( $P=0.04$ ) (Fig. 3). Non-compliance with both empiric and tailored protocols did not yield any significant results with regard to other clinical outcomes such as readmission within 30 days, C. diff infection within 30 days, graft loss within 30 days, or death within 30 days.



**Fig. 2: Proportion of patients transferred to ICU receiving compliant or non-compliant empiric antimicrobial regimen**



**Fig. 3: Length of stay of compliant vs. non-compliant treatment in patients receiving tailored antimicrobial therapy for an infectious syndrome**

## **CONCLUSION**

The impact of adherence to standard guidelines upon clinical outcomes remains the subject of much debate. Further, there is a lack of research on the efficacy of guidelines in the management of infectious syndromes in the SOT population. Our preliminary data demonstrates that non-compliance with locally developed antimicrobial management guidelines resulted in a higher proportion of patients being transferred to the ICU, as well as an increased length of stay. Future studies with a larger sample size will allow for a better assessment of short-term outcomes and will also assess long-term outcomes associated with compliance to infection management guidelines, such as tracking the development of antimicrobial resistance within a year following admission.

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