Immunomodulators did not increase secondary bacterial infections in critically ill mechanically ventilated COVID-19 patients

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Background

- The COVID-19 pandemic has caused multiple waves of infection globally causing considerable morbidity and mortality.
- Immunomodulators such as tocilizumab and baricitinib have been shown to improve survival in COVID-19 patients admitted to the hospital by countering the dysregulated host immune response to COVID-19 but may predispose the host to secondary bacterial infections (SBI).
- The association between SBI and the routine use of immunomodulators in severe COVID-19 is not fully known.

Specific Aims

- The main objective of this study is to evaluate the association between SBI and routine use of immunomodulators in severely ill COVID-19 patients.

Methods & Analysis

- This is a retrospective cohort study
- Included critically ill adults admitted to the ICU with severe COVID-19 who needed mechanical ventilation between April 2020 to December 2021 at our rural tertiary care community hospital.
- Cohort into treatment and control groups based on their exposure to immunomodulators.
- Primary outcome was the occurrence of a secondary bacterial infections during the hospital stay.
- Performed logistic regression to adjust for potential confounders between the groups.
- *Exempt study approved by NLH-EMMC IRB 2021-022-EMMC.*

Results

- In this study 168 patients were included.
- Patients did not differ in terms of demographics and co-morbidities between the two groups.
- 154 patients (92%) received systemic corticosteroids. 71 (42%) received immunomodulators, of which 42 received tocilizumab, 26 received baricitinib and 3 received both.
- Out of 81 SBI, 42 occurred in the immunomodulator group and 39 in the non-immunomodulator group.
- Immunomodulators were not associated with an increase in secondary bacterial infections compared to patients that did not receive them (Adjusted OR 1.88; 95% CI 0.90 to 3.89; P = 0.09).
- Secondary outcomes demonstrated:
  - Increase in hospital mortality (Adjusted OR 3.02; 95% CI 2.16 to 16.14; P < 0.01)
  - Decrease in hospital-free days on day 90 (-13 days; 95% CI -25 to -1 days)
  - No difference in ventilator-free days on day 28 (-3 days; 95% CI -7 to 0.1 days)

Table: Comparison of study population between treatment with and without immunomodulators

Variables		Treatment without Immunomodulators, N(97)	Treatment with Immunomodulators, N(71)	p value
Age Group	<45	6(6%)	8(11%)	0.19
	45-59	32 (33%)	28(39%)	
	60-75	37(38%)	27(38%)	
	>75	22(23%)	8(11%)	
Race	White	88(92%)	70(99%)	0.05
	Non-white	8(8%)	1(1%)	
Gender	Male	58(60%)	44(62%)	0.78
Covid Vaccination	Yes	15(17%)	10(14%)	0.66
AFib	Yes	14(14%)	10(14%)	0.95
Coronary Artery Disease	Yes	28(29%)	13(18%)	0.12
Hypertension	Yes	63(65%)	45(63%)	0.83
Diabetes	Yes	49(51%)	28(39%)	0.15
Chronic Lung Disease	Yes	48(49%)	27(38%)	0.12
Obesity (BMI =/>30)	Yes	60(62%)	53(75%)	0.081
Congestive Heart Failure	Yes	13(13%)	2(3%)	0.017
Any Malignancy	Yes	11(11%)	4(6%)	0.2
Immunosuppression	Yes	12(12%)	4(6%)	0.14
Chronic Kidney Disease	Yes	14(14%)	8(11%)	0.55
Chronic Liver Disease	Yes	6(6%)	4(6%)	0.88
Cerebrovascular Disease	Yes	9(9%)	4(6%)	0.38
O2 Therapy on Day 0	Room Air	6(6%)	1(1%)	0.11
	Low Flow	28(29%)	14(20%)	
	High Flow Nasal Canula	6(6%)	9(13%)	
	CPAP/BiPAP	55(57%)	47(66%)	
	Mechanical Ventilation	2(2%)	0(0%)	

Conclusion

- Immunomodulator therapy was not associated with an increased risk of secondary bacterial infection in our patient cohort.
- Findings are consistent with current guidelines that recommend using immunomodulators in patients with severe COVID-19.
- Although our study demonstrates an increase in hospital mortality and worse outcomes in terms of hospital-free days in patients that received immunomodulators, these findings may be due to residual confounding from probable selection of higher-severity patients for receipt of immunomodulators.

Limitations

- Small sample size
- Single-center design
- Observational nature
- Limits the generalizability of findings

Future Recommendations

- Further larger scale multi-center studies are recommended.
- Difficult to establish causation between different factors and development of SBI, due to retrospective study design

Disclosure

- None of the authors for this presentation have relevant financial relationships to disclose.

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