



Clostridium Difficile Infection Increases In-hospital Mortality, Length of Stay, and Hospital Cost but not 30-Day Mortality in Cirrhotic Patients: A Systematic Review and

Meta-Analysis

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Introduction

· Clostridium difficile infection (CDI) is a leading cause of nosocomial infection and is associated with higher morbidity and mortality

 Cirrhotic patients are more susceptible to CDI because of impaired gut immune response, frequent hospitalization, and use of proton pump inhibitor and antibiotics • We aim to investigate the impact of CDI on cirrhotic patients in terms of in-hospital and 30-day mortality, length of stay, and hospital cost

Methods and Materials

 Potentially eligible studies were identified from Embase, Medline, and Web of Sciences databases from inception to April 2022 using search strategy that comprised of terms for "cirrhosis" and "CDI"

 Eligible study must consist of one group of cirrhotic patients with CDI and control group of cirrhotic patients without CDI

 The study must provide odds ratio (OR) and 95% confidence interval (95% CI). We extracted such data from each study to calculate mean difference (MD) or OR. Pooled MD/OR were then calculated by combining MD/OR of each study using random-effects model

· Funnel plot was used to assess for the presence of publication bias

Contact

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				104.0494		Odds Ratio			Odds Ratio			
	Α.		log[Odds Ratio]			, Random, 95%			IV, Random, 95% CI			
		Bajaj 2009			11.1%	1.55 [1.29, 1.8			-			
_		Khanna 2013	0.3365		14.3%	1.40 [1.30, 1.5			· · · · · · · · · · · · · · · · · · ·			
		Patel 2016	0.6627	0.0555	13.3%	1.94 [1.74, 2.1						
		Fernandez 2018 Rosenblatt 2019	0.8256		0.8%	2.28 [0.67, 7.7 1.47 [1.40, 1.5						
		Aloreidi 2019	0.6313		14.0%	1.88 [1.79, 1.9						
		Kim 2020	0.4253		14.5%	1.53 [1.44, 1.6						
		Volcu 2021	0.8036		1.7%	2.23 [0.98, 5.1						
		Atteberry 2021	0.6907		14.8%	2.00 [1.91, 2.0				0-SE(log))R%	
							.,			0T-00-04		99
FΙ		Total (95% CI)		1	100.0%	1.68 [1.50, 1.8	9]		•			d
' I		Heterogeneity: Tau ² =	0.02; Chi ² = 141.29	J, df = 8 (P	< 0.0000 × 9	l); P= 94%		0.01	0.1 1 10 100			
		Test for overall effect .	Z = 8.78 (P < 0.000)	01)					C.diff less IPD mortality C.diff more IPD mortality	0.2		
						Mean Diff			Mean Difference			
	_	Ct	Marca 1977-1978		or 184-1-			10				8
	B	Study or Subgroup	Mean Differen			ht IV, Randoi			IV, Random, 95% Cl	0.4		0
		Bajaj 2009		7.1 0.48			.15, 8.05]					Ŭ
		Khanna 2013		5.2 0.30			.60, 5.80]					
· 1		Patel 2016		6.6 0.1			.31, 6.89]		•	0.6-		
'		Femandez 2018		65 5.71		i% 58.65 [47				0.0		0
		Rosenblatt 2019		35 0.14:			.07, 6.63]					
		Kim 2020		6.2 0.12			.95, 6.45]		•	11110		
		Volcu 2021	6.	76 1.79	63 4.2	96 6.76 [3.:	24, 10.28]	2021		0.8+		
		Total (95% CI)			100.	6.56 [5	.75, 7.36]		r			
			- 0.91: Chiž - 104	1 47 df-								· · · · ·
	Heterogeneity: Tau ² = 0.81; Chi ² = 104.47, df = 6 (P < 0.00001); i ² = 94%								-100 -50 Ó 50 100	0.01	0.1	1
		reation overall enec	10.02 (1 - 0						C.diff less LoS C.diff more LoS			
-	Mean Difference Mean Difference											
	C	Study or Subgroup	Mean Differen	ce	SE Wei	pht IV, Rando	m. 95% C	1 Year	IV. Random, 95% Cl	E		
	0.	Bajaj 2009	40.5	96 4.45	518 19.	3% 40.60 [31	87, 49.32	2009			ure 2) Funnel	
		Patel 2016	62.	45 1.9	013 20.	1% 62.45 [58	70.66.20	2016	-	betv	veen CDI in c	irrhotic patie
<u> </u>		Rosenblatt 2019	10.8	65 1.2			49, 13.24		-			
		Kim 2020	25.6								nospi	tal mortality
		Volcu 2021	0.5				0.05, 1.08		+			
		Total (95% CI)			100.	0% 27.85 [10.	41. 45.29	1	-			
		Heterogeneity: Tau ²	- 300 99: Chit- 1	2246 56								
		neterogeneity, rau	- 330.00, Off - 2	1040.00,	ui - 4 (r	- 0.00001),1 -	100.90		-50 -25 0 25 50			

Figure 1) Forest plot of the associations between CDI in cirrhotic patients and A) in-hospital mortality, B) length of stay, C) hospital cost



Test for overall effect: 7 = 3.13 (P = 0.002)

· Reduced functional capacity due to loss of muscle mass, hepatic encephalopathy, and ascites Regular endoscopy

Higher risk of acute kidney injury

-25 0 25 5 C diff less cost C diff more cost

- Immunocompromised state
- multiple infections





Results

• A total of 2.320 articles were identified. After two rounds of independent review by three investigators, nine studies reporting in-hospital mortality and three reporting 30-day mortality of cirrhotic patients with CDI versus those without CDI were included into the meta-analysis

• The meta-analysis of nine studies consisting of 7,746,126 patients revealed a significant association between CDI and in-hospital mortality in cirrhotic patients with the pooled OR of 1.68 (95%CI 1.29-1.85, I2 94%, Figure 1A). Length of stay and hospital cost were also higher in the **CDI group** (pooled MD of 6.56 days [95% CI 5.75-7.36, I2 94%, Figure 1B] and 27.85 (x \$1,000) [95% CI 10.41-45.29, I2 100%. Figure 1Cl consecutively)

• The funnel plot for the meta-analysis of the association between CDI and in-hospital mortality was fairly symmetric and was not suggestive of publication bias

• From three studies comprising of 3,694 patients, we found that CDI was not associated with 30-day mortality in cirrhotic patients (pooled OR 1.20, 95%CI 0.75-2.24, 12 74%)

Conclusions

CDI is associated with increased in-hospital mortality, length of stay, and hospital costs, but not with 30-day mortality in cirrhotic patients. Aggressive monitoring for CDI during admission is needed in this patient population

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