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Risk factors for the emergence of multidrug-resistant organisms in liver cirrhosis

Figueiredo LM; Rafael MA; Alexandrino G; Martins A; Oliveira A; Carvalho R; Santos L; Horta D; Lourenço L; Reis J; Costa M

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Presentation by

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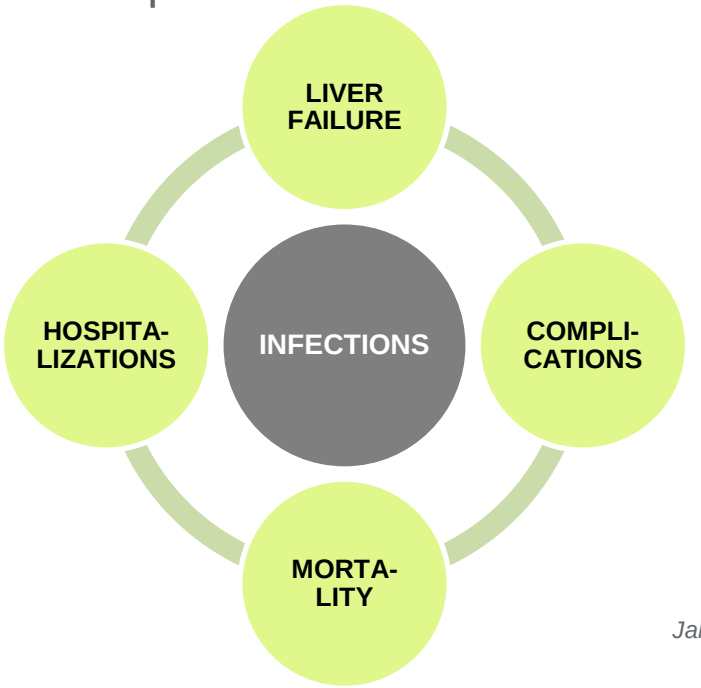
22/10/2018

Introduction

Infections in patients with liver cirrhosis (LC) are common.

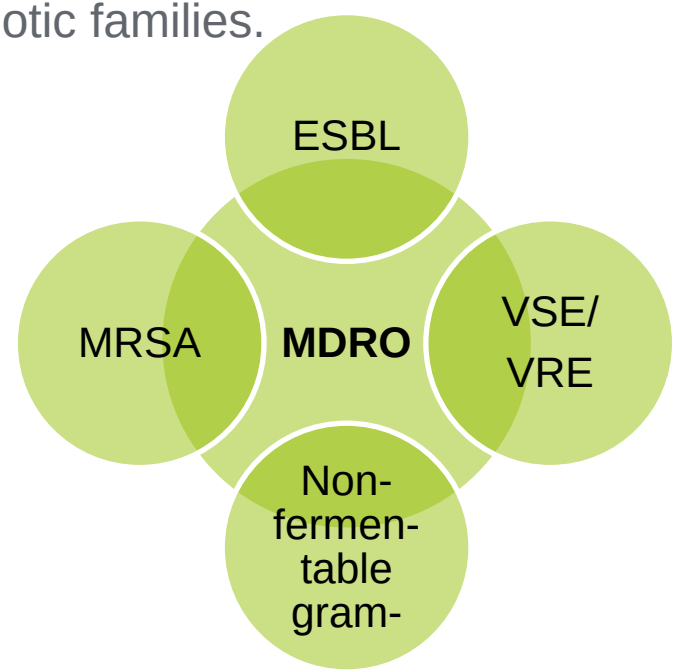


Infections are present at admission or develop during hospitalization in 25–35% of patients (4–5 fold higher compared with general population)

Jalan R et al Bacterial infections in cirrhosis Journal of Hepatology 2014; Piano S et al Infections complicating cirrhosis Liver International. 2018

Introduction

Multidrug resistant organisms (MDROs) are bacteria resistant to 3 or more of the main antibiotic families.



ESBL: extended spectrum beta lactamase producing Enterobacteriaceae

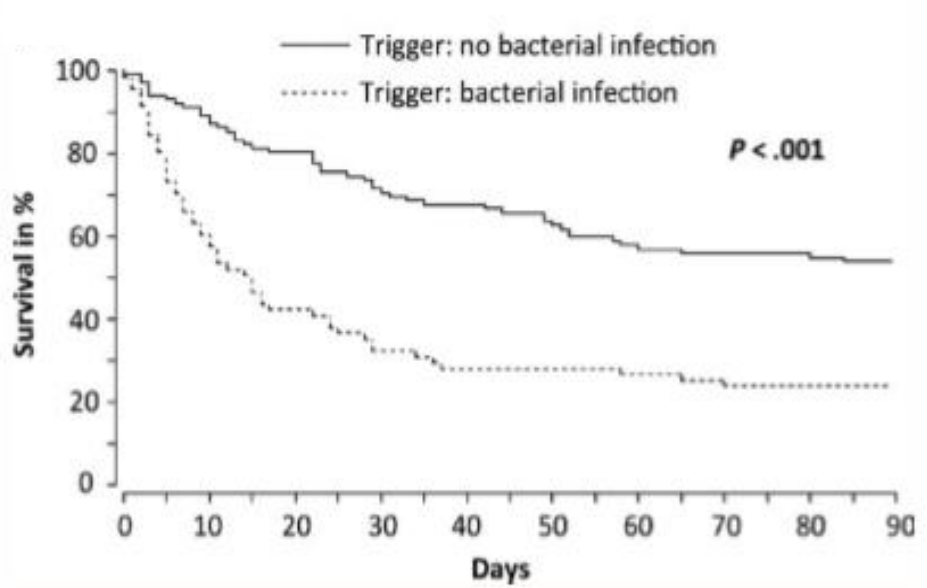
MRSA: methicillin resistant Staphylococcus aureus

VSR/VRE: vancomycin-susceptible/resistant enterococci

Jalan R et al Bacterial infections in cirrhosis: A position statement based on the EASL Special Conference 2013 Journal of Hepatology 2014; Piano S et al Infections complicating cirrhosis Liver International. 2018

Introduction

Liver cirrhosis is the 10th most common cause of death in Western world.



Overall mortality of infected cirrhotic patients is around 30% at 1 month and more than 50% at 12 months

Bartoletti M, et al Opportunistic infections in end stage liver disease Infectious Disease Reports 2017; Marcus M et al Bacterial infection-triggered acute-on-chronic liver failure is associated with increased mortality L International. 2017

Introduction

Research on risk factors of bacterial infections in cirrhosis.

Impairment of liver function
- Child-Pugh score[36-38]
- MELD score ⩾ 15[40]
- Low serum albumin[39]

Alcohol related disease[45,51]
Total ascitic fluid protein concentration < 15 g/L[84]
ICU admission[39,85]
Variceal bleeding[41,86]
- Blood transfusion requirements
- Mean arterial pressure
- Severity of bleeding

Malnutrition[40]
Invasive procedures[29]
ERCP in PSC patients or with incomplete drainage[87]
Hospitalization[29,40,43,44]

Ferrarese A et al Management of bacterial infection in the liver transplant candidate World J Hepatol 2018

Risk factor	Reference
Stage of cirrhosis / biomarkers	
Bilirubin > 3.2 mg/dl	Guarner *et al. Gastroenterology* 1999
PLT < 98000/mmc	Andreu *et al. Gastroenterology* 1993
Protein levels in ascitic fluid <1.5 g/l Child-Turcotte-Pugh >9 MELD > 19 Lymphocytes ≤ 900/mmc	Fernandez *et al. Gastroenterology* 2007 Ximenes *et al. Am J Emerg Med* 2015
Medications	
Use of PPI	O' Leary *et al. Clin Gastroenterol Hepatol* 2015
Long term exposure to antibiotics	Nahon *et al. Gut* 2015
Precipitating events	
Acute variceal haemorrhage	Bernard *et al. Hepatology* 1999
Previous infection	Fernandez *et al. Gastroenterology* 2007

Viale P, Decompensated cirrhosis Infections in cirrhotic patient viale The International Liver congress 2017 EASL Postgraduated course

Aim

Identify risk factors for the occurrence of MDROs in patients with LC.

Methods

- Prospective study **from October 2017 to March 2018**
- Consecutively hospitalized **patients with decompensated LC with infection**
- **Blood, urine and ascitic fluid** cultures were analysed
- Statistical significance: **p-value <0.0500**

Patients Analysis

52 episodes of infection | 22 patients

GENDER

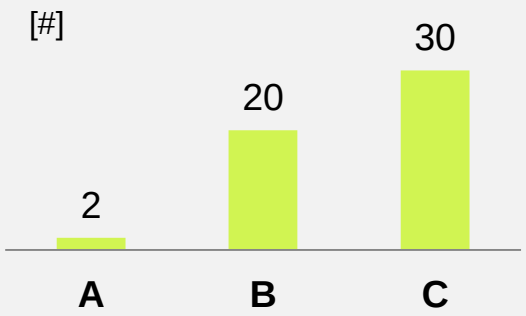
17%
Female Patients

83%
Male Patients

AGE

Average	**63.5**
Minimum	**30.0**
Maximum	**88.0**
Std. deviation	**14.4**

CHILD-TURCOTTE-PUGH SCORE



Patients Analysis

Patients Analysis

52 episodes of infection | 18 MDROs

GENDER

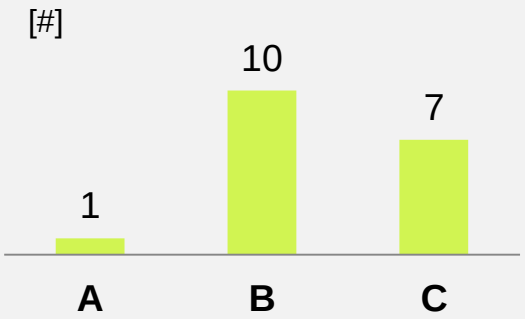
17%
Female Patients

83%
Male Patients

AGE

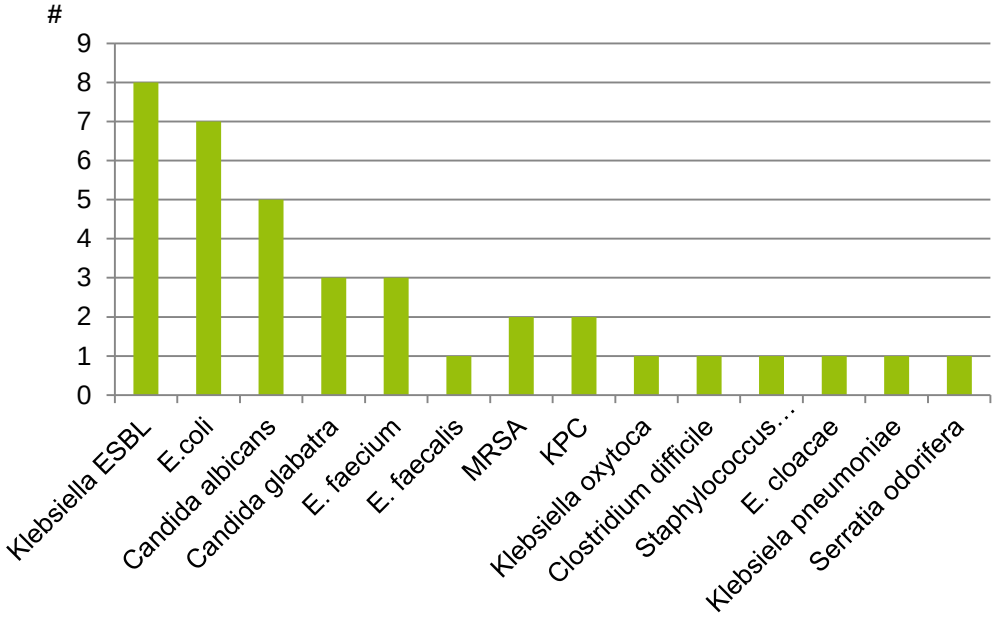
Average	**63.9**
Minimum	**30.0**
Maximum	**85.0**
Std. deviation	**12.2**

CHILD-TURCOTTE-PUGH SCORE



Patients Analysis

Number of isolated microorganisms identified



- **MDROs identified:** Klebsiella ESBL, E. faecium, E. Faecalis, MRSA, KPC, Clostridium dificile, Staphylococcus haemolyticus methicillin resistant
- **Klebsiella ESBL was the most frequently isolated MDRO – 44.4%**

Results

MDROs were significantly associated with:

RISK FACTOR	ANTIBIOTICS <90 DAYS	HOSPITALIZATION >48H / HOSPITAL DISCHARGE <30 DAYS	PROTON PUMP INHIBITORS	MORTALITY 3M
MDRO #18	94.4%	100%	72.2%	71.4%
NON MDRO #19	47.4%	68.4%	36.8%	35.7%
P-VALUE	0.0033	0.0082	0.0312	0.0316

Results

There was no MDROs relevant statistical association with:

RISK FACTOR	BLADDER CATHETER	CENTRAL VENOUS CATHETER	DIABETES MELLITUS	HEPATO-CELLULAR CARCINOMA	MORTALITY 1M
MDRO #18	61.1%	38.9%	38.9%	33.3%	27.8%
NON MDRO #19	42.1%	26.3%	31.6%	31.6%	26.3%
P-VALUE	0.2599	0.4283	0.6526	0.9124	0.9230

Conclusion

- **MDROs are a current reality that can alter the paradigm of treatment and prevention of infection in LC.**
- The indiscriminate **use of antibiotics and PPIs increases the risk of MDROs infections**, suggesting that the prescription of these drugs should be restricted to formal indication.
- **Hospitalization for more than 48 hours or hospital discharge for less than 30 days have been shown to influence the onset of MDROs**, suggesting that hospitalizations in LC patients should be limited to the minimum number of days required.

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