Covid-۱۹ ;
Gastrointestinal & liver manifestations

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Introduction

-Coronavirus ; A common source of upper respiratory , GI & CNS infections in humans

-Prevalence of GI symptoms ; ١٠-١٢%

-٣% ; only digestive system without respiratory symptoms

-GI symptoms ; worsen the outcome,

-less likely to recover & discharge

Inroduction

-ACE٢ (The cellular entry receptor of SARS-COV-٢)

-Multiple biopsies via endoscopic procedure ;

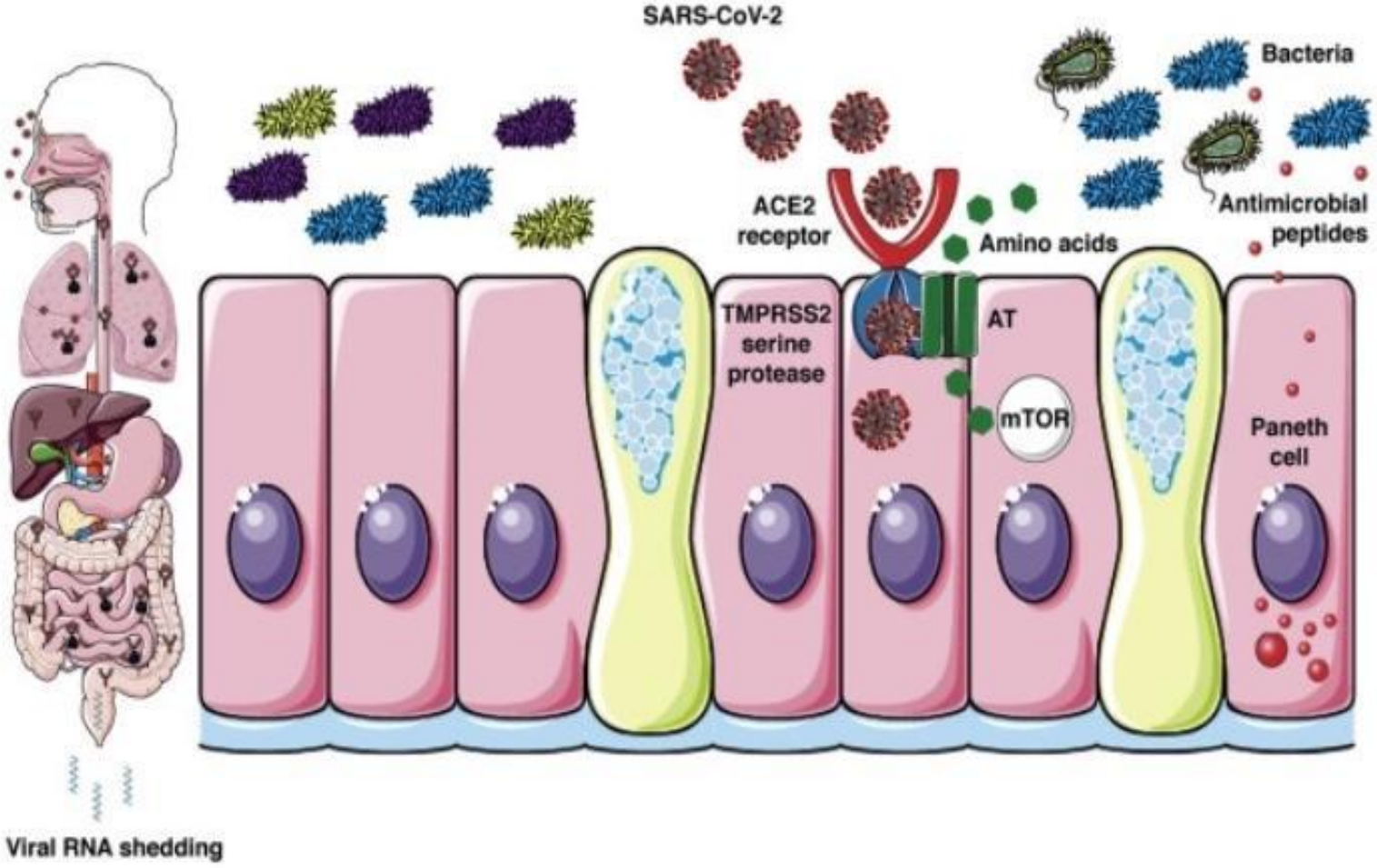
(esophagus, gastric , duodenal & rectal)

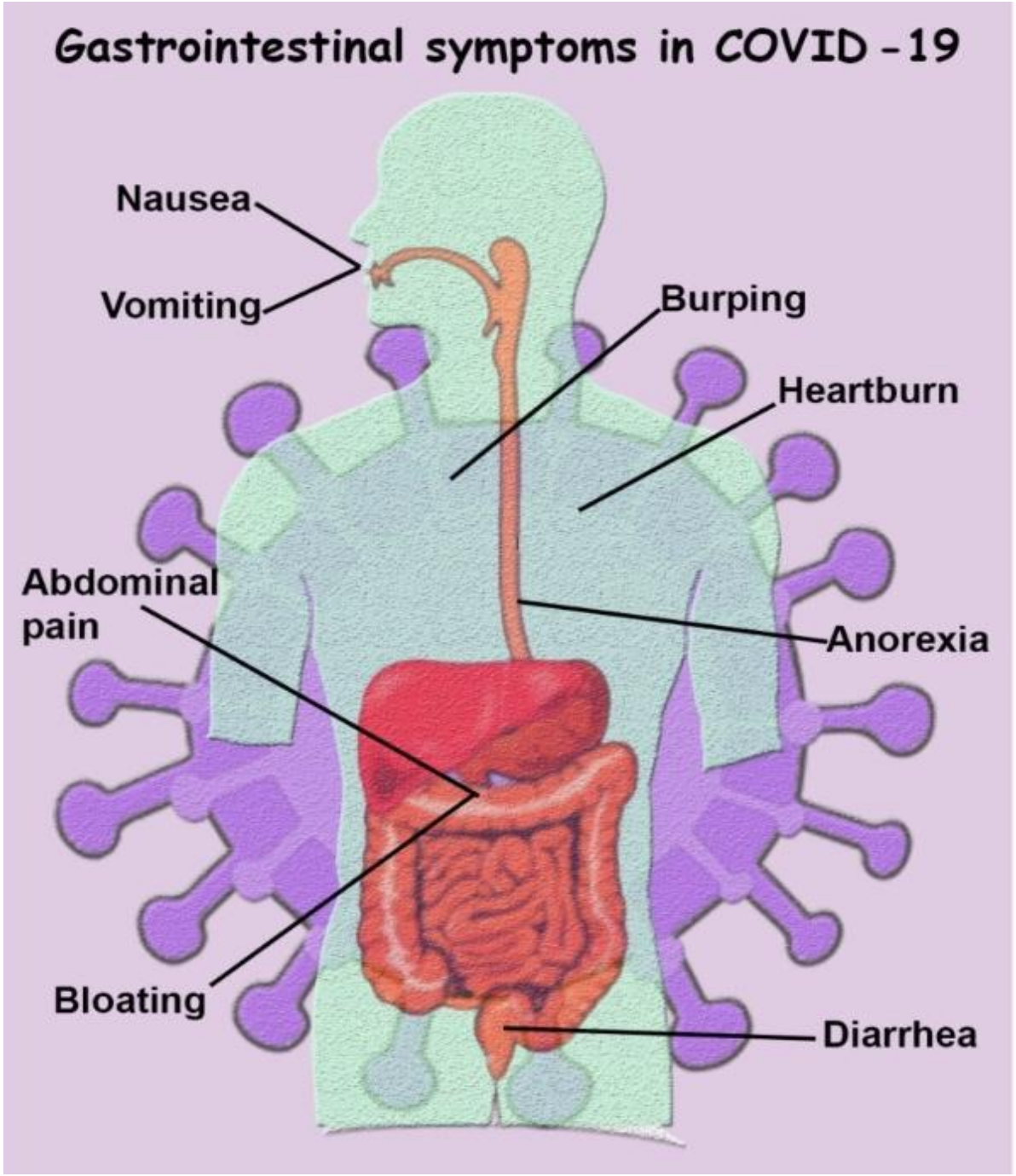
High presentation of ACE ٢ Pr in glandular cells

Inroduction

-ACE٢-epressing intestinal epithelium cells (small intestine ,proximal & distal) ; Increased risk of attack by SARS-COV-٢

-Digestive system ; A route of infection


SARS-CoV-2
Bacteria
ACE2
receptor
Amino acids
Antimicrobial
peptides
TMPRSS2
serine
protease
AT
mTOR
Paneth
cell
Viral RNA shedding


Gastrointestinal symptoms in COVID-19
Nausea
Vomiting
Burping
Heartburn
Abdominal pain
Anorexia
Bloating
Diarrhea

Introduction

Diarrhea ; ١٠%

Nausea & vomiting ; ٣-١٠%

Abd pain ; ١-٢,٢%

Elevated liver enzymes ; ٣٠%

Diarrhea

-The most prevalent presentation ; Diarrhea (٣-١٠%), (٢-٥٠%)

-Underestimation of COVID-١٩

-SARS-COV ٢ shedding in stool :٤٠ % of confirmed nasophageal swab testing or respiratory secretions (orofecal transmission)

-A median duration of ١١ days after symptom onset(delayed elimination in stool)

Diarrhea

-Positive or negative rectal viral RNA ;

No differences in GI symptoms

- No clear correlation of GI system & detectable virus in the stool

-Overal coincidence of respiratory and rectal samples ; ٧٠%

-SARS-COV-٢ RNA in rectal samples ; Longer period / higher positive rate & viral load

Diarrhea

-Intestinal microbial dysbiosis (Reduced lactobacillus & bifidobacterium) ; Probiotics

-Cytokine storm & dysregulation

Diarrhea

-ACE ٢ ; (١٠-٢٠ times higher binding affinity) compared with SARS-COV

-Alteration of intestinal permeability resulting in enterocyte malabsorption

Diarrhea

-Up to ٢٠% of patients ; positive viral RNA in stool even after negative samples of respiratory tract

-Fecal-oral transmission

-Nosocomial infection ,esp in endoscopy unit

Diarrhea

-An increasing number of cases

-May precede or trail respiratory symptoms

-Median symptom onset day; Forth

-Most nonhydrating loose stools ,average of ٣ evacuation-per day

-No cases of severe diarrhea

Diarrhea

-Greater diarrhea percentage in patients with severe disease compared with non severe ones

-& more likely to require mechanical ventilation & had ARDS (٦,٧% VS ٢ %)

Diarrhea

-No specific treatment

-Supportive care ,Rehydration & potassium monitoring

-No efficacy of antidiarrheal drugs

-Antibiotics and antivirals ; likely alteration of gut micro biota (Probiotics?)

Diarrhea

-Improvement in diarrhea after starting antiviral therapy

-Remdesevir (Prevent viral replication)

Nausea & Vomiting

-Nausea and vomiting ; Both can be early acute symptom of COVID ١٩

-Delayed hospital admission & worse clinical outcome

-Some infected subjects ; w/o classical symptoms

Nausea & Vomiting

-Mechanisms ;

Release of key hormones from the entero-endocrine cells (EEC) in GI mucosa

Activation of abd vagal afferent (in mechanoreceptors) in duodenum & jejunum

Nausea & Vomiting

-Mechanisms ;

Release of neuroactivating agent into systemic circulation to act on the area postrema

Alteration of gut microbiota

Expression of ACE٢ MRNA

Nausea & Vomiting

-Drugs

-Antibiotics & Antivirals

-Damage outside of the GI tract ;

Lung, renal failure ,liver dysfunction and cardiac failure

Hepatic Involvement

-ACE ٢; Vital role in pathogenesis of liver damage in COVID ١٩

-Highly expressed in cholangiocytes & hepatocytes (Leading to tissue hypoxia &liver injury)

-Systemic inflammatory response

Hepatic Involvement

-Alcohol, Drug history ,Obesity & history of fatty liver & chronic disease

-Male, overweight ,his of smoking : Risk factors of liver enzyme elevation

-lymphopenia, thrombocytopenia (with elevated liver enzyme level)

-Lung Radiologic presentation ; similar between patients with & w/o liver enzyme elevation

Hepatic Involvement

-Elevated AST & ALT ; ١٤-٥٨% (٢٨%) of hospitalized COVID-١٩

-Most liver enzyme elevations ; Mild

Hepatic Involvement

-Severe acute hepatitis & liver failure (even before typical symptoms of COVID-١٩) ;rare

-Often AST> ALT (associated with Dis severity) ,

-Less frequent ; Elevated ALP & Bili

-Low Alb ; associated with severe COVID-١٩

Hepatic Involvement

-Elevated PT

Hence

-close monitoring of liver function & liver enzymes in especially in digestive symptoms of COVID-١٩

Hepatic Involvement

-Liver histology ;

Nonspecific, moderate microvesicular steatosis ,mild mixed lobular ,focal & portal necrosis

Focal portal lymphocyte infiltration /suggestive of hepatic vascular involvement

Hepatic Involvement

-Diagnostic evaluation to determine the etiology of elevated liver enzymes ;

Medications

Viral hepatitis assay

Imaging ? (Unless biliary obstruction or venous thrombosis or ..)

Hepatic Involvement

-Drug toxicity ; a mechanism for covid-١٩ associated liver injury (dynamic monitoring of LFT)

-Elevated liver enzyme ; not a contraindication to use drugs such as Remdesevir

-ALT > ٥ times ULN ; Not recommended

-Remdesevir should be discontinued if it rise or liver injury happened

PPI

-A mainstay in the treatment of acid-related conditions

-Multiple studies ; association with increased risk for both infectious & noninfectious conditions

-Twice daily PPI ;significantly increases risk compared to once daily

-H٢ blocker

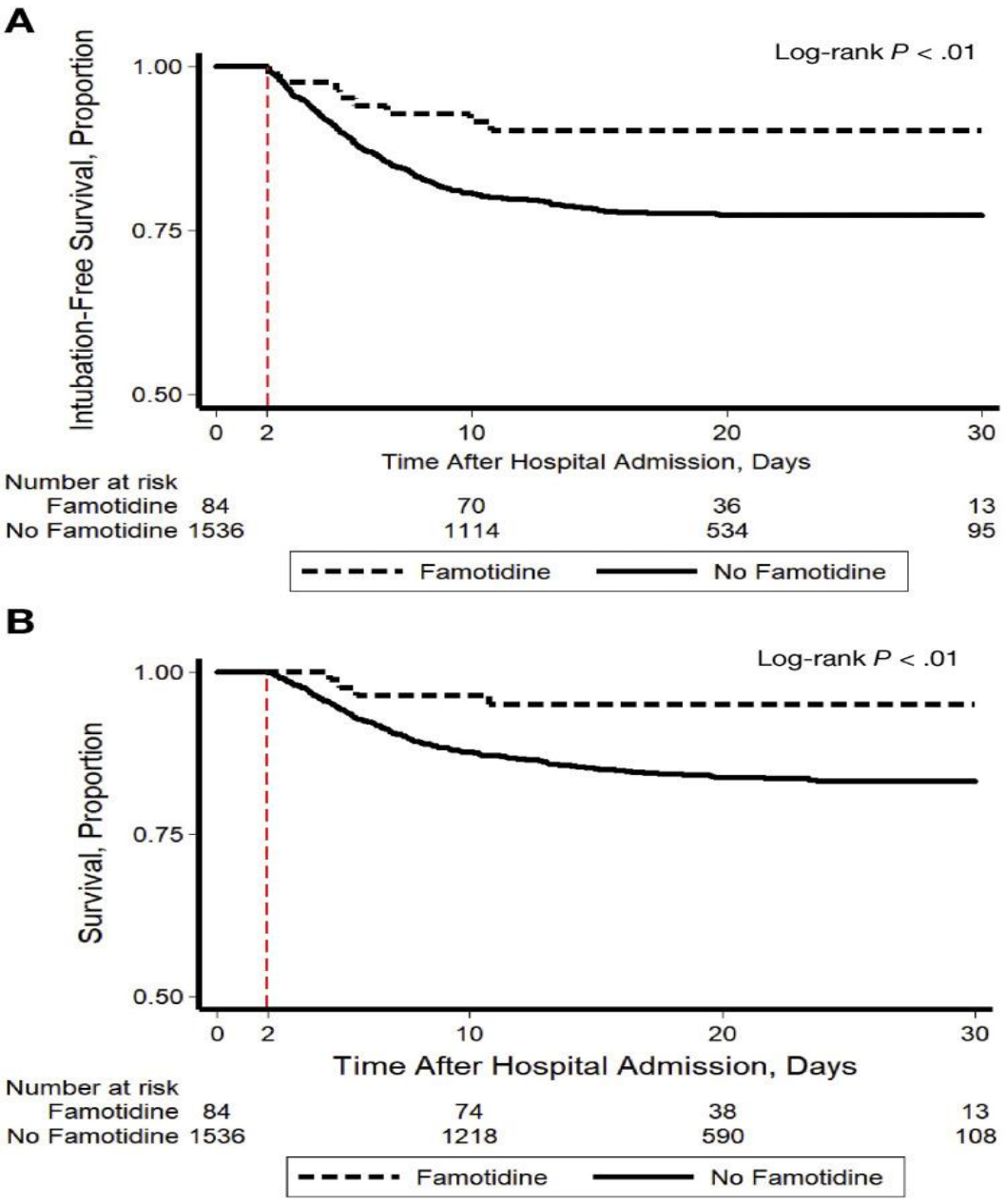
Famotidine

-Histamine receptor anatagonist

-٢-fold reduction in deterioration, leading to intubation or death in hospitalized cases

-Blocking viral replication & reduction the cytokine storm during COVID ١٩

Famotidine Use Is Associated With Improved Clinical Outcomes in Hospitalized COVID-١٩ Patients: A Propensity Score Matched Retrospective Cohort Study


A
Log-rank P < .01
Intubation-Free Survival, Proportion
1.00
0.75
0.50
0
2
10
20
30
Time After Hospital Admission, Days
Number at risk
Famotidine 84 70 36 13
No Famotidine 1536 1114 534 95
Famotidine
No Famotidine
B
Log-rank P < .01
Survival, Proportion
1.00
0.75
0.50
0
2
10
20
30
Time After Hospital Admission, Days
Number at risk
Famotidine 84 74 38 13
No Famotidine 1536 1218 590 108
Famotidine
No Famotidine

Famotidine

-Do not support evidence of in-hospitalized famotidine use on reduced mortality in patients

-No association between in-hospitalized-famotidine use & ٣٠-days mortality after adjustment

Famotidine Use Is Not Associated With ٣٠-day Mortality: A Coarsened Exact Match Study in ٧١٥٨ Hospitalized COVID-١٩ Patients from a Large Healthcare System

Take home message

-Attention to isolated GI symptoms as a potential COVID-١٩

-More severe disease course and worsening outcome in GI tract & hepatic symptoms